See the corresponding editorial in this issue, pp 103–105.

J Neurosurg (2 Suppl Pediatrics) 106:106–110, 2007

Intelligence quotient in children with meningomyeloceles: a case–control study

Farideh Nejat, M.D., M.P.H.,[1] Syed Shuja Kazmi, M.D.,[1] Zohreh Habibi, M.D.,[2] Parvin Tajik, M.D.,[3] and Zahra Shahrivar, M.D.[4]

[1]Department of Neurosurgery, Children's Hospital Medical Center, Tehran University of Medical Sciences; [2]Department of Neurosurgery, Iman Khomeini Hospital, Tehran University of Medical Sciences; [3]Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences; and [4]Department of Psychiatry, Roozbeh Hospital, Tehran University of Medical Sciences, Tehran, Iran

Object. Meningomyelocele (MMC) is a common central nervous system birth defect. As one of many problems facing patients with MMC, learning disabilities are often overlooked. The aim of this study was to evaluate IQs in a group of children with MMCs and determine if a correlation exists between intelligence level and the presence of an MMC and/or its complications.

Methods. A case–control study was conducted at the Children's Hospital Medical Center in Tehran, Iran, from December 2004 through December 2005. The patient group included 50 children with MMC from 5 to 12 years of age who were referred to the authors' institution for treatment of complications or for follow up after surgery for MMC closure. The patient group was individually matched for age and sex with a control group of 50 children referred to the hospital for other reasons and who did not have MMC or other neurological abnormalities. The IQs in all children in this study were evaluated using the Ravens Progressive Matrices test.

The children in both groups were similar in the socioeconomic status of the family ($p = 0.347$) and educational status of the father ($p = 0.117$) and mother ($p = 0.439$). Patient age at the time of surgery for MMC closure varied from 1 day to 96 months (mean 4.1 months). Only 20% of the patients with MMC could walk with a normal gait. Forty-six percent of the patients had undergone placement of a ventriculoperitoneal shunt, and half of these patients experienced shunt-related complications; 72% of the children in the patient group were completely incontinent for both urine and feces. The IQ results obtained in the patient group ranged from 73 to 134 with a mean ($\pm$ standard deviation) of 96.62 ± 13.01. In the control group the IQ range was 70 to 128, and the mean was 104.82 ± 12.30. Compared with the control group there was a statistically significant correlation between having an MMC and having a lower IQ ($p < 0.001$, paired t-test).

Conclusions. Although the average IQ in the patient group was significantly lower than that in the control group, it is important to note that all children in the patient group had an average or above-average IQ. In contrast with the results reported in other studies, earlier repair of the MMC, the presence of a shunt or shunt-related complications, walking difficulty, and the spinal level of the lesion did not correlate significantly with IQs. Therefore, the lower IQ and reduced cognitive levels noted in these patients result from the disease process itself and not from the associated complications.

Key Words • hydrocephalus • meningomyelocele • intelligence quotient • shunt • pediatric neurosurgery

Meningomyelocele is one of the most serious developmental disabilities[1] with an incidence of 1.6 per 1000 live births.[9] More children are currently crippled by MMC than by muscular dystrophy, traumatic paraplegia, or poliomyelitis.[13] Meningomyelocele is so diverse that no single theory can be cited to explain all forms of spinal dysraphism, although a deficiency in maternal dietary folate has been postulated as a cause.[1] Meningomyelocele results from a failure of primary neurulation during Days 18 through 27 of human embryogenesis.[6] Meningomyeloceles have been reported at all spinal levels: lumbosacral in 30% of cases, thoracolumbar in 26%, lumbar in 26%, sacral in 10%, thoracic in 5%, and cervical in 3% of cases.[1]

Hydrocephalus is commonly associated with MMC and develops in 80 to 90% of patients with this anomaly; its incidence varies according to lesion location.[1] Other abnormalities associated with MMC include paresis of the lower extremities with associated gait disturbance or paraplegia, Chiari malformation, vertebral anomalies, genitourinary dysfunction, epilepsy, and ophthalmological complications. These morbidities affect the physical, social, emotional, and

Abbreviations used in this paper: DSM-IV-TR = Diagnostic and Statistical Manual of Mental Disorders, IV-Revised; MMC = meningomyelocele; RPM = Ravens Progressive Matrices; WAIS-R = Wechsler Adult Intelligence Scale, Revised.

cognitive development of almost all children with MMCs. Whether these complications affect the mental development and IQ in these children is still debated.

The mental development of every child depends on multiple factors, including genetic predisposition, family care and support, nutrition, and home environment.[7] There has been little research about the mental development and functioning of children with MMCs in Iran and other developing countries. We used the RPM test to evaluate the IQs in children with MMCs and the children in a control group.

Clinical Material and Methods

Participant Selection

A case–control study was conducted in the Children's Hospital Medical Center in Tehran from December 2004 to December 2005. The patient group was composed of 50 children, 5 to 12 years of age, who were referred to our institution for treatment of an MMC and associated complications. The control group consisted of 50 children referred to our hospital for nonneurological reasons (such as incontinence, vesicoureteral reflux, undescended testes, hypospadias, bone fractures or other orthopedic problems, and acute abdominal pain) who were individually matched by age (± 6 months) and sex with the children in the patient group. Consent for participation in this study was obtained from the parents of all children in both groups. Variables such as parents' educational status, family socioeconomic level, ambulatory status of the patients, and bladder and bowel continence are shown in Table 1.

TABLE 1

*Summary of the basic characteristics of patient and control groups**

Variable	No. of Patients (%)	No. of Control Volunteers (%)	p Value
parents' educational status			
father			0.117†
no HS diploma	28 (56)	36 (72)	
HS diploma	16 (32)	10 (20)	
>HS diploma	6 (12)	4 (8)	
mother			0.439†
no HS diploma	33 (66)	36 (72)	
HS diploma	12 (24)	11 (22)	
>HS diploma	5 (10)	3 (6)	
family's socioeconomic status			0.347†
good	12 (24)	18 (36)	
can provide basic needs	27 (54)	21 (43)	
cannot provide basic needs	11 (22)	11 (22)	
child's attention status			0.18‡
attentive	35 (70)	41 (82)	
inattentive	15 (30)	9 (18)	

* HS = high school.
† According to the Wilcoxon signed-rank test.
‡ According to the McNemar test.

Testing Procedures

The RPM test was conducted to evaluate IQ in all children in both groups with either the colored progressive matrices (in children 5–8 years of age) or standard progressive matrices (in children ≥ 8 years of age). The scores obtained from the RPM test gave a measure of the general intelligence of each child. Although these scores are significantly increased with advancing years of education and higher socioeconomic status,[8] this test is a good indicator of conceptual ability because the responses elicited from the participant require neither verbalization and skilled manipulative abilities nor subtle differentiation of visuospatial information.[18] The RPM test is generally accepted as the quintessential tool to assess inductive reasoning, but it cannot be used to assess performance and verbal IQs separately as do the WAIS-R and Stanford–Binet tests.[7]

Choosing the most appropriate test was crucial because it was the most important variable in this study. Despite the availability of highly developed and widely accepted tests such as the WAIS-R, Stanford–Binet, and Kaufman,[8] the RPM test was selected because of its availability and ease of implementation. Moreover, most children included in this study did not have a sufficient attention span for the other, more time-consuming tests. After testing, each child's IQ was categorized as below normal, normal, or above normal according to the DSM-IV-TR guidelines.

The participants' level of attentiveness was identified as a confounding factor in the evaluation of IQ. We therefore devised a method to evaluate each child's level of attentiveness during testing. Although attentiveness cannot be quantified precisely, the interviewer was instructed to evaluate each child's level of attentiveness by estimating the frequency of distraction from the test. The interviewer would also periodically ask each child to justify the reasoning behind his or her response. In this way the interviewer could determine whether the children were answering carelessly in hopes of ending the test sooner or actually paying attention.

Statistical Analysis

Because the cohorts were individually matched, the data were analyzed using the paired t-test, McNemar, and Wilcoxon signed-rank tests with the aid of statistical software (SPSS version 11.5; SPSS, Inc.). To evaluate the effect of MMC on IQ and to control for other probable confounding factors, a linear regression curve for panel data was created using commercially available software (Stata, version 8; StataCorp).

Results

The patient group included 26 boys and 24 girls who were matched with a control group of children; all participants were between 5 and 12 years of age (mean 7.3 ± 2.0 years [values are presented as means ± the standard deviations]). The educational level of the parents and the socioeconomic status of each child's family for both cohorts are shown in Table 1. Matched data analysis demonstrated no statistically significant difference in attentiveness between the two groups ($p = 0.18$). In the patient group only 35 patients (70%) were attentive during the testing process and in the control Group 41 patients (82%) were attentive.

The IQ results in the patient group ranged from 73 to 134 points (mean 96.6 ± 13.0) and in the control group the range was 70 to 128 points (mean 104.8 ± 12.3). When the mean IQ of the patient group was compared with that of the control group by using the paired t-test, a probability value of less than 0.001 was obtained. The IQ results obtained in both groups were categorized according to the DSM-IV-TR

TABLE 2

Comparison of patient and control group IQs

IQ Range	DSM-IV-TR Classification	No. of Patients	No. of Healthy Volunteers
70–79	borderline	5	1
80–90	dull normal	11	6
90–110	normal	26	25
110–120	bright normal	7	15
120–130	superior	0	3
>130	very superior	1	0

classification, which revealed that 90% of children in the patient group and 98% of children in the control group had an IQ within the normal or above normal range (Table 2).

To investigate the confounding effect of inattention during testing, we evaluated the association between the IQ and level of attentiveness in these children. The mean estimated IQ was 103.9 ± 12.1 in attentive children and 90.7 ± 11.9 in inattentive ones, confirming a statistically significant association ($p < 0.001$) between attentiveness and measured IQ. To control for the effect of attentiveness on the association between MMC and IQ, we performed a conditional linear regression for matched data by using Stata-8 software. The parameters of this model are presented in Table 3. The model demonstrates that the presence of MMC and the attentiveness of the child during the test are independent predictors of IQ. After controlling for the effect of attentiveness during the IQ test, we found that a low IQ is still associated with the presence of MMC.

To find the possible determinants of low IQ in patients with MMC we compared the IQs in different subgroups of patients (categorized by the main disease characteristics) using univariate statistical analysis (Table 4). No statistically significant association was observed between sex, MMC location, incontinence, or the ambulatory status of each child and his or her IQ.

All patients except one had undergone surgery for MMC closure. The procedure was performed in these patients when they were between 1 day and 96 months of age (mean 4.1 ± 15.1 months). To evaluate the effect of patient age at the time of surgery on IQ, we divided the patients into two groups: those who had undergone surgery when they were younger than 1 month of age, and those who had undergone surgery when they were 1 month of age or older. No statistically significant difference in their IQs was found ($p = 0.12$). A ventriculoperitoneal shunt had been placed in 23 patients (46%). Patient age at the time of shunt placement varied from 4 days to 96 months (mean 7.5 ± 19.78 months). Neither the presence of a shunt nor its complications was found to have a statistically significant correlation with the patient's IQ.

TABLE 4

*Correlation between IQ in patients with MMC and possible determining characteristics**

Characteristic	No. of Patients (%)	IQ (mean ± SD)	p Value
sex			0.56†
male	26 (52)	97.6 ± 13.7	
female	24 (48)	95.5 ± 12.5	
MMC location			0.69‡
thoracic	1 (2)	98.0	
thoracolumbar	8 (16)	95.7 ± 13.0	
lumbar	16 (32)	95.6 ± 11.5	
lumbosacral	15 (30)	94.4 ± 16.1	
sacral	10 (20)	102.1 ± 11.1	
continence status			0.71‡
total continence	3 (6)	99.3 ± 10.1	
daytime bladder & bowel continence	3 (6)	92.3 ± 12.1	
daytime bowel continence only	8 (16)	91.4 ± 13.8	
totally incontinent	36 (72)	97.9 ± 13.2	
ambulatory status			0.76‡
wheelchair bound	17 (34)	95.7 ± 15.9	
ambulatory w/ long brace	4 (8)	90.0 ± 14.3	
ambulatory w/ short brace	3 (6)	93.3 ± 19.6	
ambulatory w/ help & abnormal gait	16 (32)	98.3 ± 10.1	
ambulatory w/o help & normal gait	10 (20)	99.1 ± 10.7	
shunt status			0.37†
does not have shunt	27 (54)	98.1 ± 13.9	
has shunt	23 (46)	94.8 ± 12.0	
w/ complications	11 (48)	97.9 ± 11.9	0.25†
w/o complications	12 (52)	92.0 ± 11.8	

* SD = standard deviation.
† According to the Student t-test.
‡ According to the one-way analysis of variance.

Discussion

The birth of a child with an MMC is challenging for the parents.[3] An MMC in a newborn can be particularly difficult for the whole family, a drain on the financial resources of the family and society, and pose an unrewarding challenge to the medical profession. If treated early enough, however, most children with an MMC will survive to reach adulthood. The primary worries of the parents are related to the prospects for the child's survival, ambulation, and intellectual development.[1] The incidence of this highly crippling malformation is much higher in Iran (1.6/1000 live births)[10]

TABLE 3

*Parameters of the linear analysis of panel data made using the general equation estimation population-averaged model**

Independent Variable	Regression Coefficient	Standard Error	z Score	p Value	95% CI
group	−6.81453	1.999643	−3.41	0.001	−10.73376 to −2.895301
attentiveness	−11.54559	2.708836	−4.26	0.000	−16.85481 to −6.236364
constant	118.4438	3.583573	33.05	0.000	111.4201 to 125.4675

* Number of observations 100, number per group 50, Wald $\chi^2 = 35.44$, scale parameter 131.2427, $p \geq 0.0000$ (chi-square test). Abbreviation: CI = confidence interval.

than in more developed countries.[6] Although authors of prior studies have reported a female predominance in MMC,[6] 52% of our patients were boys. In previous studies conducted in Iran, the investigators have also reported a 52 to 56% male predominance.[9,10,14] This may indicate a different sex predominance in the incidence of MMC in this geographic region than in the rest of the world. Moreover, in other countries, MMCs are reported most often in the lumbosacral region (30%) and least frequently at the cervical level (3%).[1] In the present study, however, the most prevalent spinal level for MMC was the lumbar region (32%), and the least prevalent was the thoracic (2%) region.

Parents always ask whether their child will have normal mental development or whether the presence of the anomalies associated with MMC will require the child to attend a school for children with special needs. The IQs in patients with MMC have been reported to be less than that of the general population but within the range of normal.[2,4,11,19,20] We report mean IQs of 96.62 $\pm$ 13.01 in patients with MMC and 104.82 $\pm$ 12.30 in the patients in the control group—a statistically significant difference ($p < 0.001$). We observed that although the mean IQs in the patient group were less than those in the control group, the IQs were in the average range according to DSM-IV-TR classification[16] and none of our patients scored at the level of mental retardation. A statistically significant association was found between attentiveness during testing and the mean IQ obtained within the patient group ($p = 0.001$) and the control group ($p = 0.013$), but the level of attentiveness was similar for both groups ($p = 0.180$). Even when attentiveness is included as a confounding factor, the mean IQ results obtained in patients with MMCs were lower than those obtained in the control group.

In examining the intellectual development of any person, a number of parameters have to be considered apart from the raw IQ. An individual's IQ is determined by multiple factors including genetic predisposition and environmental factors such as early home environment and education.[7] With these variables in mind, we compared the two cohorts by focusing on the educational qualifications of parents and the socioeconomic level of the families, confirming that both groups were comparable for these factors. We found no statistically significant association between the mean IQ in either group and the educational levels of the parents or the socioeconomic level of the families. These results may be influenced by inadequate or misleading information provided by the parents during testing or by improper classification of the educational qualifications or socioeconomic levels in our questionnaire.

In a study by Beeker et al.,[3] surgery for MMC closure was performed in 85% of cases during the first 24 to 36 hours of life; in their patients in whom surgery was not undertaken death occurred within the first 2 years of life. Closure of the MMC was performed in our patients only at their parents' request; the mean age at closure was 4.1 $\pm$ 15.1 months. Among our patients, 8% had had meningitis before primary MMC closure. There was no statistically significant difference between the mean IQs of patients treated early and those treated later.

Among patients harboring lesions at high locations in the spine, the proportion of children with normal intelligence is lower than those harboring lesions at lower spinal locations. It has been reported that the likelihood of mental retardation increases with MMCs located at higher sites on the spine.[5] Among our patients, those who had an MMC at a higher spinal level had a mean score of 96.0 $\pm$ 19.2, whereas those with a lesion located lower along the spine had a mean score of 96.75 $\pm$ 13.30. There was no statistically significant difference between the IQs in these two groups. Hydrocephalus is present in 80 to 90% of patients with MMCs. Variations in its incidence occur with the spinal level of the lesion, with a higher incidence of hydrocephalus reported for lesions located higher in the spine.[1] The authors of some studies have reported that patients with MMC and accompanying hydrocephalus have a 10% lower IQ than the general population, and that early and effective management of this anomaly leads to a higher IQ. These authors have noted that when patients with or without hydrocephalus were similarly matched, those with hydrocephalus scored lower on intelligence tests.[4,17,19] Cohen and Robinson[5] have argued that shunt placement and its related complications (infection, obstruction, and the need for shunt revision surgery) play a greater role in the decreased mean IQ in patients with MMC than the hydrocephalus itself. We found no correlation, however, between the IQs of patients with MMCs who had undergone shunt placement and those who had not. This finding is in accordance with the results reported by Ralph et al.,[15] Mirzai and colleagues,[13] and Beeker et al.[3]

Only 46% of our patients underwent shunt placement, and their mean age at the time was 7.5 $\pm$ 19.8 months. There was a large difference between the mean age at sac repair and at shunt insertion. In contrast to the nearly 80% rate of shunt placement reported in other studies,[6] our results and those of another study from our institution[13] demonstrated a very low rate of shunt placement. Shunt placement had been undertaken in only a limited number of patients and not in all patients in whom it was indicated. There are many reasons for this mismanagement. The low socioeconomic status of families, most coming from remote areas of Iran, makes it difficult for them to afford the surgery. Many doctors do not like to work on disabled patients and so they postpone the surgery because of the risk. Moreover, when shunts are placed, complications are prevalent,[1] developing in 47.8% of our patients who received shunts. There was no significant correlation between these complications and the mean IQ level in our study population.

To our knowledge, there are no previous reports on IQs of patients with MMCs and the correlation with their ambulatory/continence status and IQ. In our patients no significant differences were found between the mean IQ of ambulatory and nonambulatory children, or continent and incontinent children. We believe that these factors play a lesser role in the level of IQ than previously thought.

It is important to note that assessment of IQ can only be done in patients who have survived. The cultural and socioeconomic status of the child's family and the country are determinants of which patients will survive. In Iran there is no general agreement on treatment protocols for patients with MMCs, and no specific governmental or nongovernmental support system for children with MMCs and their families. Therefore, the decision to treat the child is left to the parents, and physicians do not have an active role in this decision. Some parents request early treatment, others postpone treatment, and some never seek treatment for their children. Consequently, there is a wide range in the ages of

children at the time of surgery for MMC closure or shunt placement and for treatment of associated complications of MMC in our study population.

In more developed countries, there is a consensus that children with MMC should be treated aggressively and that such treatment will benefit most, if not all, affected children, although it has been accepted that no criteria can successfully predict which children will have a favorable long-term result.[6,12] Because of the heterogeneity of patient populations, differences in treatment regimens, and variations in the tests used to evaluate intelligence, IQ levels among patients with MMCs vary significantly throughout the literature. Moreover, higher IQ results are obtained in better treatment settings and hydrocephalus and the other related factors have been postulated as possible reasons for lower IQs,[9,11,13,16,17] but this effect has only been observed for general and verbal scores. When performance and calculation ability were also evaluated using other IQ tests such as the WAIS, Stanford–Binet, and California Verbal Learning Tests, IQs of almost all these patients were lower than those of developmentally normal children. This finding was true even in patients with MMCs but no shunt infections, who had not undergone shunt revision surgery, and in those in whom there had been no other complications. As seen in our study and also reported in the studies by Mirzai et al.[13] and Beeker and colleagues,[3] this suggests that IQ is affected predominantly by the presence of the MMC itself and not by its associated complications. This finding was also true in patients with lower-than-average IQs.

Conclusions

Despite the fact that the mean IQ in the patient group was significantly lower than that measured in the control group, it is important to note that all patients with MMCs demonstrated an average or higher-than-average IQ. Contrary to the results of some studies, we found that the earlier repair of an MMC, the presence of hydrocephalus requiring shunt placement, shunt complications, difficulty in walking, continence status, and the spinal level of the lesion do not have statistically significant correlations with IQ. Therefore, the lower IQ and cognitive level observed in these patients results from the disease process itself and not the associated complications.

References

1. Akar Z: Myelomenincele. **Surg Neurol 43:**113–118, 1995
2. Beeker TW: Factors related to intelligence in myelomeningocele. **Eur J Pediatr Surg 8 (1 Suppl):**73–76, 1998 (Abstract)
3. Beeker TW, Scheers MM, Faber JA, Tulleken CA: Prediction of independence and intelligence at birth in meningomyelocele. **Childs Nerv Syst 22:**33–37, 2006
4. Casari EF, Fantino AG: A longitudinal study of cognitive abilities and achievement status of children with myelomeningocele and their relationship with clinical types. **Eur J Pediatr Surg 8 (1 Suppl):**52–54, 1998
5. Cohen AR, Robinson S: Early management of myelomeningocele, in McLone DG (ed): **Pediatric Neurosurgery: Surgery of the Developing Nervous System, ed 4.** Philadelphia: WB Saunders, 2001, pp 241–260
6. Cohen AR, Robinson S: Myelomeningocele and myelocystocele, in Winn HR (ed): **Youmans Neurological Surgery, ed 5.** Philadelphia: WB Saunders, Vol 3, 2004, pp 3215–3228
7. Gleitman H: Intelligence: its nature and measurement, in **Psychology, ed 4.** New York: W W Norton & Co, 1995, pp 581–624
8. Kaplan RM, Saccuzo DP: **Psychological Testing: Principles, Applications and Issues, ed 4.** Pacific Grove, CA: Brooks/Cole Publishing Co., 1997, pp 256–361
9. Kazmi SS, Nejat F, Tajik P, Roozbeh H: The prenatal ultrasonographic detection of myelomeningocele in patients referred to Children's Hospital Medical Center: a cross sectional study. **Reprod Health 18:**3–6, 2006
10. Ketabchi S, Ghodsi SM, Nejat F: Incidence of gross nervous system anomalies in newborns at two obstetric centers in Tehran. **J Med Council Iran 18:**277–281, 2001
11. Kinsman SL, Rawlins C, Finney K, Ruffing V, Speedie L: A conceptual model of higher cortical function impairments in myelomeningocele. **Eur J Pediatr Surg 8 (1 Suppl):**69–70, 1998
12. McLone DG, Czyzewsky D, Raimondi AJ, Sommers RC: Central nervous system infections as a limiting factor in the intelligence of children with myelomeningocele. **Pediatrics 70:**338–342, 1982
13. Mirzai H, Ersahin Y, Mutluer S, Kayahan A: Outcome of patients with meningomyelocele, the Ege University experience. **Childs Nerv Syst 14:**120–123, 1998
14. Nejat F, Kajbafzadeh AM, Tajik P, Kazmi SS: Urologic evaluations of myelomeningocele patients: a study in Children's Hospital Medical Center in Tehran, in **13th World Congress of Neurological Surgery, Marrakesh, Morocco, June 19–24.** Brussels: World Federation of Neurosurgical Societies, 2005, pp 179–192
15. Ralph K, Moylan P, Canady A, Simmons S: The effects of multiple shunt revisions on neuropsychological functioning and memory. **Neurol Res 22:**131–136, 2000
16. Sadock BJ, Sadock VK: Clinical neuropsychological testing, in **Synopsis of Psychiatry: Behavioral Sciences/Clinical Psychiatry, ed 9.** Philadelphia: Lippincott Williams and Wilkins, 2003, pp 178–192
17. Soare PL, Raimondi AJ: Intellectual and perceptual-motor characteristics of treated myelomeningocele children. **Am J Dis Child 131:**199–204, 1977
18. Spreen O, Strauss E: **A Compendium of Neuropsychological Tests: Administration, Norms, and Commentary, ed 2.** New York: Oxford University Press, 1998, pp 83–89
19. Tew B, Laurence KM: The effects of hydrocephalus on intelligence, visual perception and school attainment. **Dev Med Child Neurol Suppl 35:**129–134, 1975
20. Wills KE, Holmbeck GN, Dillon K, McLone DG: Intelligence and achievement in children with myelomeningocele. **J Pediatr Psychol 15:**161–176, 1990

Manuscript submitted August 15, 2006.
Accepted November 1, 2006.

Address reprint requests to: Farideh Nejat, M.D., Children's Hospital Medical Center, Tehran University of Medical Sciences, Tehran, Iran. Mailbox: Tehran, F. Nejat, 14155-7854. email: nejat@sina.tums.ac.ir.