Analysis of Denver Neurodevelopmental Screening Test Results of Myelomeningocele, Hydrocephalus, and Microcephaly Patients

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Context: Spina bifida, hydrocephalus, and similar congenital central nervous system (CNS) anomalies take origin from embryologic stages weeks before birth, but assessment and follow-up of these patients are important to figure and predict the effects of these anomalies on child’s neurodevelopment. Aims: To evaluate of multiple groups of congenital CNS anomalies in the neurodevelopment level. Settings and Design: The study was conducted at a research and treatment center for spina bifida patients. Materials and Methods: The study group included 348 patients with a mean age of 15.4 (±15.1) months, who had spina bifida aperta, hydrocephalus, and microcephaly. Patients with other known intracranial conditions were excluded. The subjects were evaluated into five groups: Group 1, 88 patients with congenital hydrocephalus; Group 2, 48 patients with congenital hydrocephalus and ventriculoperitoneal shunt; Group 3, 148 patients with microcephaly; Group 4, 30 patients who were operated for spina bifida aperta; and Group 5, 39 patients who were operated for spina bifida aperta and also had ventriculoperitoneal shunt implantation. Denver Developmental Screening Test II was used to assess patients’ neurodevelopment levels. Statistical Analysis Used: Pearson’s chi-square and Fisher’s exact tests were used for data analysis. Group comparisons were also made in pairs with chi-square test according to Bonferroni corrections. Frequency of abnormal findings was significantly correlated with age (P = 0.014). Results: Total score differences of five groups appeared to be statistically significant according to Pearson’s chi-square test (P = 0.000). When we compared groups in pairs, abnormal results were significantly frequent in shunted groups (P < 0.01). Conclusions: Our results suggested that shunt-dependent hydrocephalus caused serious neurodevelopmental impairments in patients.

Keywords: Denver Neurodevelopmental Screening Test, hydrocephalus, microcephaly, neurodevelopment, spina bifida, ventriculoperitoneal shunt

INTRODUCTION

In terms of neurodevelopment, early childhood is an important period.¹⁻³ Spina bifida and hydrocephalus are the most frequent congenital anomalies affecting the central nervous system (CNS), and therefore, has a huge effect on neurodevelopment of patients.⁴⁻⁵ Most of the time spina bifida is also accompanied by hydrocephalus.⁶ Disturbance in patient’s neurodevelopment results with retardation in patient’s cognitive, motor, and language skills.

In hydrocephalus patients, callosal dysgenesis, white matter erosion on periventricular areas, slight shifts of basal ganglia and tracts because of the effects of increase in ventricular volume, and cerebrospinal fluid pressure are suggested mechanisms to explain neurodevelopmental alterations.⁶⁻⁸ In spina bifida patients, to explain motor

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impairments on upper extremities, apart from the lower extremity deficits, it is suggested that accompanied posterior fossa and cerebellum anomalies might be responsible for decreased organization of fine and gross motor movements of arms and hands. In 1993, Bushnell and Boudreau explained an important concept named “haptic perception” in their study, suggesting children's ambulation level and ability to reach and examine objects by hands have a contribution to visual and cognitive development, in addition to motor development. This concept shows us the complexity of neurodevelopmental stages and clarifies unpredicted effects of many anomalies on child's development in addition to CNS anomalies.

Spina bifida, hydrocephalus, and similar congenital CNS anomalies take origin from embryologic stages weeks before birth, but assessment and follow-up of these patients are important to figure and predict the effects of these anomalies on child's neurodevelopment. In our study, we aimed to evaluate and compare multiple groups of congenital CNS anomalies in terms of neurodevelopment level.

**MATERIALS AND METHODS**

**Study population**

This study was conducted in Spina Bifida Research and Treatment Center, Istanbul Bilim University, Florence Nightingale Hospital. The study population includes 348 patients with mean age of 15.4 (15.1) months, who were operated and/or followed up in our institution for spina bifida aperta, hydrocephalus, and microcephaly. Only patients who had been diagnosed with these CNS anomalies were included. Patients with other known intracranial conditions (tumor, arachnoid cyst, holoprosencephaly, etc.) were excluded. Written informed consent was obtained from carers of all patients.

**Study design**

The subjects were evaluated into five groups.

Group 1 consisted of 88 patients with mean age of 17.5 (14.76) months, who had congenital ventriculomegaly without spina bifida, and were followed up, and not operated.

Group 2 included 48 patients with mean age of 13.6 (12.7) months, had congenital hydrocephalus without spina bifida, and had undergone ventriculoperitoneal (VP) shunt surgery.

Group 3 included 143 microcephaly patients with mean age of 14.7 (14.5) months, who were followed up.

Group 4 consisted of 30 patients with mean age of 15.2 (18.6) months, who were operated for spina bifida aperta.

Group 5 included 39 patients with mean age of 15.4 (18.1) months, operated for spina bifida, and had undergone VP shunt surgery for accompanied hydrocephalus.

In our institute, myelomeningocele, hydrocephalus, and microcephaly patients constitute the majority of patients. As an instrument to assess and compare these patient groups’ neurodevelopment levels, we chose Denver Developmental Screening Test II (DDST), and the efficacy of DDST in these patient groups was observed. DDST includes a series of age-specific questions and an evaluation chart to assess patients’ responses under social, fine motor, language, and gross motor subheadings. On this evaluation chart, questions and expected observations were indicated with percentages, according to patients’ age in months. It shows us if the child's development level is below the level of other children of the same age. According to the guideline, a patient receives a “caution” when failing on an item that matches 75%–90% with the age, and patient receives a “delay” when failing on an item that matches 90% or beyond with the age. When patient denied an item, outcomes are assessed for each of the four subgroups. When one delay or two or more cautions are received, the subject's performance is considered questionable. If there are two or more delays, the result is considered abnormal. For a total score, patient’s results in subgroups are assessed with the same rule as normal, abnormal, and questionable (“questionable” results are calculated just as “caution”).

The medical ethical review board of our hospital approved the study and all participants gave their written informed consents. Parents or caretakers of all subjects under the age of 18 gave written permission for the adolescents to participate.

Calculations were made using SPSS 22.0 (IBM Inc., Chicago, IL). Pearson's chi-square and Fisher's exact tests were used for data analysis, and $P < 0.05$ was accepted as significant. Group comparisons were also made in pairs with chi-square and Fisher's exact tests, and $P < 0.001$ was accepted as significant according to Bonferroni corrections.

**RESULTS**

Three hundred and forty-eight patients with spina bifida aperta (myelomeningocele), hydrocephaly, and microcephaly (137 female, 217 male) were evaluated. Mean age was 15.4 (15.1) months and the range was 0–88 months. Of these, 137 patients were born by caesarean delivery and 217 were born by normal delivery (Table 1). As we examine the mode of delivery according to groups, significantly higher rates of cesarean delivery...
was observed in spina bifida and hydrocephalus groups than microcephaly group (49.1%) as predicted.

The scores of the DDST is as follows: 134 (38.5%) subjects had normal, 136 (39%) subjects had abnormal, and 78 (22.4%) subjects had questionable results. No significant relationship was found between abnormal results and gender (P = 0.729) nor the mode of delivery (P = 0.341). Between consanguinity degree and frequency of abnormal results, we observed almost an invert ratio (first degree: 54.2%, second degree: 30%, third degree: 0, no consanguinity: 35.7%), but the relationship was not significant according to Fischer’s exact test (P = 0.057). To evaluate abnormal result correlation with age, we divided the patients into three groups based on their age: 0–24, 24–48, and >48 months. The abnormal results were higher in >48 group and we found that the ratio of abnormal results was significantly increasing proportionally with age (0–24, 36.5%; 24–48, 41.9%; >48, 66.6%) (P = 0.014) [Table 1].

Each group’s test results were assessed under subheadings of personal-social, fine motor, language, and gross motor development, and their total scores were calculated afterward [Table 2]. In total results, abnormal finding rates of groups were assessed as 36.4%, 70.8%, 27.3%, 13.3%, and 69.2%, respectively. Total score differences of five groups appeared statistically significant according to Pearson’s chi-square test (P = 0.000). On comparing in pairs, 7 comparisons out of 10 revealed as significantly different (significant P value was determined as <0.01, according to Bonferroni correction) [Table 3]. The highest developmental delays were in Group 5 and Group 2, in which all subjects had VP shunts. When we further analyze our results according to subheadings, in Table 2, we found out that worst development scores in gross motor and fine motor areas belonged to Group 5, and worst scores in social and language areas belonged to Group 2. The least delayed development scores were observed in Group 4, which consisted of patients who were operated for only spina bifida. Best gross motor development among the subjects was seen in Group 3, the microcephaly group.

**DISCUSSION**

Our results showed that operated spina bifida group (Group 4) has best results, but we think this particular patient group could achieve higher results because these patients have fallen behind of social interaction from the early stages of life. We suggest that the alteration in test scores might be caused by non-organic reasons. With education and social interaction with the peers, these scores may rise.

Group 2 consisted of congenital hydrocephalus patients without spina bifida, who had undergone VP shunt surgery. In this group, causes of the hydrocephalus are various. Because of this, other reasons that may affect the DDST results were ignored.

There were no significant differences between hydrocephalus (Group 1) and microcephaly (Group 3) groups. The presence of VP shunt has a great impact on neurodevelopment in every aspect. Comparisons between Group 1 vs 2 and 4 vs 5, both revealed a significant

### Table 1: Clinical and social profile of study group

| Variables        | Normal (n,%) | Abnormal (n,%) | Questionable (n,%) | Total (n) | P       |
|------------------|-------------|---------------|-------------------|-----------|---------|
| Gender           |             |               |                   |           |         |
| Female           | 56 (40.9)   | 52 (38)       | 29 (21.2)         | 137       | 0.729*  |
| Male             | 78 (37)     | 84 (39.8)     | 49 (23.2)         | 211       |         |
| Consanguinity    |             |               |                   |           |         |
| 1st Degree       | 17 (35.4)   | 26 (54.2)     | 5 (10.4)          | 48        | 0.057** |
| 2nd Degree       | 3 (30)      | 3 (30)        | 4 (40)            | 10        |         |
| 3rd Degree       | 1 (50)      | 0             | 1 (50)            | 2         |         |
| None             | 100 (41)    | 87 (35.7)     | 57 (23.3)         | 244       |         |
| Mode of delivery |             |               |                   |           |         |
| N.D.             | 58 (44.3)   | 47 (35.9)     | 26 (19.8)         | 131       | 0.341*  |
| C.S.             | 76 (35)     | 89 (41)       | 52 (24)           | 217       |         |
| Age (months)     |             |               |                   |           |         |
| 0–24             | 123 (41.9)  | 107 (36.5)    | 63 (21.5)         | 293       | 0.014*  |
| 24–48            | 8 (23.8)    | 13 (41.9)     | 10 (32.3)         | 31        |         |
| >48              | 3 (12.5)    | 16 (66.6)     | 5 (20.8)          | 24        |         |

N.D. = normal delivery, C.S. = caesarean section

*Pearson chi-square test (significant P value < 0.05)

**Fisher’s exact test (significant P value < 0.05)
decrease in DDST scores \( (P = 0.001 \text{ and } P = 0.000, \text{ respectively}) \), whereas the comparison between Group 2 and 5 did not reveal any significant difference [Table 3].

In 2011 and 2013, Hampton et al. presented two informative studies that evaluate the effect of shunt in neurodevelopment scores in hydrocephalus and spina bifida patients.\(^{[6,13]}\) In the first study, they evaluated the effect of shunt on spina bifida patients. They separated groups as only spina bifida patients, spina bifida patients with arrested hydrocephalus, and spina bifida patients with VP shunt. As predicted, there was a linear proportion between developmental delay and hydrocephalus level, but the differences were reported as not significant.\(^{[6]}\) In our study, there is a very significant difference between these study groups. In the latter study, they evaluated and compared 29 congenital hydrocephalus patients with aqueductal stenosis, treated with shunt, and 141 myelomeningocele patients with shunt-dependent hydrocephalus.\(^{[13]}\) They reported a significant difference in cognitive, motor, and memory domains according to their neurodevelopment instrument. In our groups with shunts (Groups 2 and 5), we found only a slight difference \( (P = 0.987) \) [Table 3].

In an earlier study, Lomax-Bream et al. had followed 91 spina bifida patients for 36 months.\(^{[4]}\) During follow-up, 77 of these patients underwent VP shunt surgery, and as a result of the evaluation, they reported a significant regression in motor and cognitive development in the presence of shunt. As compatible with Lomax-Bream’s results, in our shunted study groups (Groups 2 and 5) we received abnormal results with very high ratio in gross motor domain as 72.9% and 79.5%, respectively.

### Table 2: Denver Developmental Screening Test results

| Group | 0 | Abnormal | Normal | Questionable | Total |
|-------|---|----------|--------|--------------|-------|
|       | N | %        | N      | %            | N     |
| 1     | Pers_Social | 1 | 1.1 | 23 | 26.1 | 61 | 69.3 | 3 | 3.4 | 88 | 100.0 |
|       | Fine_motor | 6 | 6.8 | 37 | 42.0 | 44 | 50.0 | 1 | 1.1 |
|       | Language   | 2 | 2.3 | 27 | 30.7 | 57 | 64.8 | 2 | 2.3 |
|       | Gross_motor| 0 | 0.0 | 42 | 47.7 | 43 | 48.9 | 3 | 3.4 |
|       | Total score| 32 | 36.4 | 29 | 33.0 | 27 | 30.7 |
| 2     | Pers_Social | 0 | 0.0 | 27 | 36.3 | 19 | 39.6 | 2 | 4.2 | 48 | 100.0 |
|       | Fine_motor | 1 | 2.1 | 31 | 64.6 | 13 | 27.1 | 3 | 6.3 |
|       | Language   | 0 | 0.0 | 23 | 47.9 | 25 | 52.1 | 0 | 0.0 |
|       | Gross_motor| 0 | 0.0 | 35 | 72.9 | 12 | 25.0 | 1 | 2.1 |
|       | Total score| 34 | 70.8 | 7 | 14.6 | 7 | 14.6 |
| 3     | Pers_Social | 1 | 0.7 | 31 | 21.7 | 106 | 74.1 | 5 | 3.5 | 143 | 100.0 |
|       | Fine_motor | 3 | 2.1 | 40 | 28.0 | 97 | 67.8 | 3 | 2.1 |
|       | Language   | 3 | 2.1 | 36 | 25.2 | 104 | 72.7 | 0 | 0.0 |
|       | Gross_motor| 0 | 0.0 | 43 | 30.1 | 94 | 65.7 | 6 | 4.2 |
|       | Total score| 39 | 27.3 | 77 | 53.8 | 27 | 18.9 |
| 4     | Pers_Social | 2 | 6.7 | 1 | 3.3 | 27 | 90.0 | 0 | 0.0 | 30 | 100.0 |
|       | Fine_motor | 2 | 6.7 | 5 | 16.7 | 23 | 76.7 | 0 | 0.0 |
|       | Language   | 2 | 6.7 | 2 | 6.7 | 26 | 86.7 | 0 | 0.0 |
|       | Gross_motor| 1 | 3.3 | 11 | 36.7 | 17 | 56.7 | 1 | 3.3 |
|       | Total score| 4 | 13.3 | 15 | 50.0 | 11 | 36.7 |
| 5     | Pers_Social | 0 | 0.0 | 19 | 48.7 | 16 | 41.0 | 4 | 10.3 | 39 | 100.0 |
|       | Fine_motor | 0 | 0.0 | 26 | 66.7 | 12 | 30.8 | 1 | 2.6 |
|       | Language   | 1 | 2.6 | 14 | 35.9 | 24 | 61.5 | 0 | 0.0 |
|       | Gross_motor| 1 | 2.6 | 31 | 79.5 | 7 | 17.9 | 0 | 0.0 |
|       | Total score| 27 | 69.2 | 6 | 15.4 | 6 | 15.4 |

### Table 3: Comparison of groups as pairs

| Group | 1v2 | 1v3 | 1v4 | 1v5 | 2v3 | 2v4 | 2v5 | 3v4 | 3v5 | 4v5 |
|-------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| p     | 0.011 | 0.649 | 0.024 | 0.03 | 0.000* | 0.000* | 0.497 | 0.009 | 0.001* | 0.000* |
| f     | 0.011 | 0.024 | 0.066 | 0.035 | 0.000* | 0.000* | 0.668 | 0.027 | 0.000* | 0.000* |
| l     | 0.137 | 0.225 | 0.033 | 0.761 | 0.01 | 0.000* | 0.316 | 0.043 | 0.395 | 0.15 |
| g     | 0.018 | 0.026 | 0.283 | 0.02 | 0.000* | 0.013 | 0.448 | 0.14 | 0.000* | 0.003 |
| T     | 0.001* | 0.007* | 0.053 | 0.003* | 0.000* | 0.000* | 0.987 | 0.061 | 0.000* | 0.000* |

*p = personal-social, f = fine motor, l = language, g = gross motor, T = total. *Pearson chi-square test, \( P < 0.01 \) is significant according to Bonferroni correction.
In an interesting study, Muen and Bannister examined specifically the hand functions in spina bifida patients and reported that meningomyelocele patients with VP shunt have significantly weaker hand skills. This study supports the findings that neurodevelopmental delays cannot be simply explained by anatomic or radiological findings, there is more complex relation between child’s experience and development as it is in haptic perception concept. 

In literature, there are studies about hydrocephalus and spina bifida concomitance and their effects on neurodevelopment subdomains but there is no study comparing the neurodevelopmental outcome of microcephy patients with hydrocephalus or spina bifida patients. Cheong et al. followed 227 preterm infants and 65 microcephaly patients spotted at the end of year 2 and reported significant cognitive and motor delay in these patients. In a more recent multicentered study, Hagen et al. evaluated 660 microcephaly patients and reported 61%–74% intellectual disability and 34%–57% cognitive impairment ratio in their study groups. In our study, from our group of 143 microcephy patients, we received 27.3% abnormal and 53.8% normal results, which was a better score than the score of hydrocephalus (Group 1) and VP shunt groups (Groups 2 and 5). Abnormal result rates were 21.7% on personal-social domain, 28% on fine motor, 25.2% on language, and 30.1% on gross motor domains. Also, our microcephy group had the highest normal result with 53.8%.

To clarify “the presence of shunt” condition, we should indicate that these patients underwent shunt surgeries because of their high and dangerous levels of hydrocephalus. Basically, their health status was already worse than the patients with spina bifida and mild hydrocephalus who do not need VP shunt. Effects of these severe conditions on neurodevelopmental delay should not be ignored and the distinction must be made correctly. Resch et al. had given a good example for this situation in their study about hydrocephalus periventricular hemorrhage. They had reported significantly worse neurodevelopmental results in the shunted group, but also had indicated that there had been more grade 4 hemorrhage cases in the shunted group than the non-shunted group. One of the main limitations of these studies is that they fail to explain this cause and effect relationship. Further comparative studies with more specific patient groups might help to enlighten these relationships.

As we mentioned before, myelomeningocele, hydrocephalus, and microcephy patients constitute the majority of patients in our clinic and this study can be improved by adding other major pediatric conditions such as cerebral palsy. With the use of DDST in different patient groups, place of DDST in pediatric neurosurgery might be further discussed.

**Conclusion**

Influential mechanisms of congenital CNS anomalies on the development of cognitive, motor, and language domains have not yet been fully enlightened. In a search of a treatment with fewer complications, VP shunts are still the most functional tools in treating hydrocephalus patients. As a result of our evaluation, we observed severe neurodevelopmental delay on shunt-dependent spina bifida and shunt-dependent hydrocephalus patients. Relatively, we obtained mild neurodevelopmental impairment scores from microcephy patients.

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**Conflicts of interest**
There are no conflicts of interest.

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