Incidence of congenital hydrocephalus and the role of the prenatal diagnosis

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Abstract

Objective: To investigate the increasing incidence of hydrocephaly at the Hospital CAISM-UNICAMP and to identify its probable causes.

Methods: All children with hydrocephaly delivered at CAISM from September 1987 to December 1998 were studied. Those children presenting hydrocephaly due to neural tube defects were excluded. Data were collected from medical records of the Perinatal Genetics Sector (CAISM). Hydrocephaly incidence and statistical trend were analyzed using the Cochran-Armitage test.

Results: During the study, 111 infants with hydrocephaly (3.16/1,000 births) were identified. The annual incidence shows a significant increasing trend of hydrocephaly cases (p = 0.001). This phenomenon has been more evident since 1992. After classifying hydrocephaly in four subgroups (i.e., isolated hydrocephaly, hydrocephaly associated with congenital infection, syndromic hydrocephaly, and hydrocephaly associated with multiple defects), only isolated hydrocephaly cases show a significant increasing trend (p = 0.001). Ultrasonographic prenatal diagnosis was performed in most hydrocephaly cases (85%, 94/111). In this group, 66% of the cases were transferred to CAISM because of the diagnosis of hydrocephaly.

Conclusion: The present study strongly suggests that the increasing trend of hydrocephaly at CAISM might be related to the ultrasonography prenatal diagnosis. The subsequent referral of these cases to CAISM is due to the fact that this center is located in a Reference Hospital. Finally, among the hydrocephaly clinic groups, the increasing trend is specially observed in the etiological heterogeneous group of isolated hydrocephaly.


Introduction

Ultra-sound screening (USS) has been allowing ever earlier intra-uterine diagnoses of congenital defects (CD) and has been used as the primary diagnosis method for tracking CD within the population.1 As a consequence of the increased use of USS, by obstetricians, both for routine and for high-risk pregnancies, the detection of fetal anomalies has increased. Hydrocephalus, in particular, is being diagnosed ever earlier.

Hydrocephalus, in the past identified by a cephalic perimeter more than two standard deviations from average, is nowadays defined as a clinical entity characterized by a disturbance of the cerebrospinal circulation causing intraventricular accumulation of cerebrospinal fluid, resulting in progressive ventricular dilation.2 Hydrocephalus is generally the consequence of an obstruction of the cerebrospinal circulation, which can occur in a number of different places: in the Foramen of Monro, in the aqueduct...

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Material and methods

Data was obtained from the files of the Perinatal Genetic Program at CAISM, by review of the ECLAMC records, relating to the CAISM Maternity Unit, and of the Perinatal Genetic Clinic (PGC). Further to these sources, the hospital records of newborns and/or mothers were also reviewed. The period under study was from September 1987 to December 1998.

CLAMC has a hospital-based clinical and epidemiological program of investigation, which has recorded newborns suffering from congenital malformations, and also controls paired for gender, all from South American maternity units since June of 1967. All live births, irrespective of weight, and stillbirths of 500g or more are registered.

The hydrocephalus group was clinically classified into 4 subgroups: isolated hydrocephalus, hydrocephalus associated with congenital infections, hydrocephalus associated with dysmorphic syndromes and hydrocephalus associated with other congenital defects having no definite clinical and etiological diagnosis (with multiple malformations).

During the period, hydrocephalus incidences and tendencies were analyzed, employing the Cochran-Armitage tendency test. Cephalic perimeter at birth was also analyzed with the intention of investigating eventual differences related to prenatal diagnosis. This variable was studied separately: 1) for the group of newborn hydrocephalus sufferers refered with anterior diagnosis and those newborns whose referrals were due to other motives than hydrocephalus and 2) during the periods from 1987 to 1991 and from 1992 to 1998. The time based cut is from the point at which prenatal diagnosis by ultrasound was intensified and the Fetal Medicine Service began to be projected at the CAISM. For the comparison of averages of position and distribution of cephalic perimeter the Mann-Witney test was used and, for percentile distribution, Fisher’s exact test.

The project plan was approved by the Commission for Research and Ethics of CAISM-UNICAMP.

Results

During the period studied (September/1987 to December/1998), a total of 35,112 births were observed, of which 2,015 presented one or more (CD) congenital defects, and of these, 111 presented hydrocephalus, therefore the incidence of CD at the CAISM was 5.74% and that of hydrocephalus was 3.16/1,000 births.

The 111 cases of hydrocephalus were classified as follows: 38 cases of isolated hydrocephalus, 23 cases of hydrocephalus associated with congenital infection, 16 cases associated with dysmorphic syndromes, 34 multiple malformation cases. In addition to these, 54 cases of hydrocephalus secondary to NTCD were observed during the period studied, although not included in this sample.

of Sylvius, the Foramen of Magendie, the Foramen of Luschka or the subarachnoid space. Its etiology can be linked to genetic or environmental factors or could even be multifactorial. Autosomal recessive inheritance has been proposed in a number of cases of family recurrence.3 Recessive inheritance linked to the X has been known to be associated with stenosis of the Aqueduct of Sylvius,4 and occurs in around 2% of congenital hydrocephalus patients.5

Hydrocephalus is considered congenital when diagnosed at birth or soon afterwards, or, as has been happening more recently, during the pre-natal period. Hydrocephalus is one of the easiest anomalies to detect during the prenatal period, its diagnosis may be made from the second trimester of pregnancy onwards by means of evaluation of the size of the ventricles, the size of the ventricle atrium and their relationship to the choroid plexus.6

From a clinical and dysmorphological point of view, hydrocephalus cases can be divided between those that are isolated and those which are associated with other congenital defects (CD). The isolated ones, in general, can be the result of or related to malformations of the CNS or to congenital infections, especially toxoplasmosis.

Clinical cases of multiples malformations with no clinical etiological definition may be found among hydrocephalus patients who have associations with other congenital defects (with multiple malformations) and also cases associated with dysmorphic syndromes. More than 400 syndromes, with greatly diverse etiologies, have hydrocephalus within the constellations of their clinical findings.7,8 Another group which can also be considered is that of hydrocephalus secondary to neural tube closure defects (NTCD), which are generally analyzed separately, as they belong to a relatively well-defined category.

The incidence of hydrocephalus varies between 0.3 and 1.0/1,000 births.1,9-14 These variations could be related to ethnic and geographical differences in addition to methodological differences such as patients from a hospital or populational base, the inclusion or exclusion of stillbirths and the inclusion or not of hydrocephalus resulting from NTCD.

According to data released in the most recent final documents of the Latin American Collaborative Congenital Deformity Study (ECLAMC - Estudo Colaborativo Latino Americano de Malformações Congêgnitas) program, of which the Center for Integral Women’s Health Care (CAISM - Centro de Atenção Integral à Saúde da Mulher) at UNICAMP has been a member since September 1987, an increase in certain major congenital defects including hydrocephalus has been observed during recent years. This increase has mainly occurred in University hospitals, as is the case of CAISM, which is a university based tertiary care maternity unit and the local center of excellence.15,16

With the objective of identifying factors possibly related to the increase in hydrocephalus incidence, particularly with respect of prenatal diagnosis, the newborn population at the CAISM Maternity Unit, was studied for 11 years.

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The 111 cases of hydrocephalus were classified as follows: 38 cases of isolated hydrocephalus, 23 cases of hydrocephalus associated with congenital infection, 16 cases associated with dysmorphic syndromes, 34 multiple malformation cases. In addition to these, 54 cases of hydrocephalus secondary to NTCD were observed during the period studied, although not included in this sample.
The annual and total incidence values for hydrocephalus and the subgroups are shown in Table 1 and a graphical representation of the general incidence of hydrocephalus can be seen in Figure 1. The tendency to increase observed in the hydrocephalus group, particularly from 1992 onwards, was significant (p = 0.001). When this group was subdivided into the clinical types listed above, only the isolated hydrocephalus group demonstrated a significant increase (p = 0.001).

In relation to the variables studied in the 111 hydrocephalus cases, an average birth weight was found of 2,606g (SD = 925), average maternal age of 24 (SD = 6.1), average paternal age of 28.1 years (SD = 7.5), sex ratio 0.9:1, a multiple birth incidence of 1.8% and a 2.2% incidence of parental consanguinity. There was predominance of first time mothers (46.8%) and of caesarian deliveries (58.7%). The average gestational age at which diagnosis occurred was at 28.6 weeks (SD = 5.4). The average cephalic perimeter at birth was 36.2cm, with 55.4% of cases above the 90th percentile. The average gestational age at birth was 36.6 weeks.

Ninety-one point one percent (92/111) of the 111 newborns carrying hydrocephalus had started prenatal care at another service and referred to the CAISM due to a diagnosis of hydrocephalus (68 cases) or for other reasons (four cases for fetal anomalies and 20 cases for maternal pathologies). In 11 cases the prenatal care provider is not known, the mothers arrived at the CAISM for delivery.

Incidence tendencies were analyzed for the subgroup of hydrocephalus patients referred because of prenatal diagnosis of hydrocephalus and also for the subgroup of patients referred for other reasons, amongst which the 11 cases referred for delivery only are included. Both showed significant tendencies to increase (p = 0.001 and p = 0.043, respectively).

In 94 cases (85.5%), the diagnosis of hydrocephalus occurred during the prenatal period, in 6 (5.5%) it was immediately after delivery and in 10 (9.1%) post natal. With relation to auxiliary exams 102 (92.7%) pregnant mothers underwent prenatal USS, 75 (70.8%) newborns were subjected to transfontanelle USS and 34 (32.7%) to cranial TC. The karyotype exam, by cordocentesis or post natal, was performed in 57 (54.8%) cases.

### Table 1 - Annual and total incidence, per 1,000 births, of hydrocephalies and subgroups (isolated hydrocephaly, hydrocephaly associated with congenital infection, hydrocephaly associated with dysmorphic syndromes and multiple malformations) - between September 1987 and December 1998, at the maternity hospital of CAISM

<table>
<thead>
<tr>
<th>Year</th>
<th>HC inc.</th>
<th>Isolated</th>
<th>Congenital</th>
<th>Syndromic</th>
<th>Multiple malformations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1987</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>1988</td>
<td>1.81</td>
<td>0.45</td>
<td>0.90</td>
<td>0.00</td>
<td>0.45</td>
</tr>
<tr>
<td>1989</td>
<td>0.72</td>
<td>0.36</td>
<td>0.00</td>
<td>0.00</td>
<td>0.36</td>
</tr>
<tr>
<td>1990</td>
<td>2.46</td>
<td>0.00</td>
<td>0.70</td>
<td>0.00</td>
<td>1.76</td>
</tr>
<tr>
<td>1991</td>
<td>1.91</td>
<td>0.64</td>
<td>1.27</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>1992</td>
<td>1.85</td>
<td>0.93</td>
<td>0.31</td>
<td>0.31</td>
<td>0.31</td>
</tr>
<tr>
<td>1993</td>
<td>4.24</td>
<td>1.13</td>
<td>0.28</td>
<td>1.13</td>
<td>1.70</td>
</tr>
<tr>
<td>1994</td>
<td>4.61</td>
<td>1.44</td>
<td>0.58</td>
<td>1.15</td>
<td>1.44</td>
</tr>
<tr>
<td>1995</td>
<td>4.44</td>
<td>0.74</td>
<td>1.48</td>
<td>0.74</td>
<td>1.48</td>
</tr>
<tr>
<td>1996</td>
<td>3.58</td>
<td>1.30</td>
<td>0.65</td>
<td>0.65</td>
<td>0.98</td>
</tr>
<tr>
<td>1997</td>
<td>3.39</td>
<td>1.70</td>
<td>0.57</td>
<td>0.28</td>
<td>0.85</td>
</tr>
<tr>
<td>1998</td>
<td>5.50</td>
<td>2.75</td>
<td>0.83</td>
<td>0.55</td>
<td>1.38</td>
</tr>
<tr>
<td>Total</td>
<td>3.16</td>
<td>1.09</td>
<td>0.66</td>
<td>0.46</td>
<td>0.97</td>
</tr>
</tbody>
</table>
The average of cephalic perimeter (37.7 cm) was significantly greater among the group of hydrocephalus patients referred with previous diagnosis (p = 0.007). There was also a predominance of cephalic perimeters above the 90th percentile (38 cases) in this subgroup, when compared with the subgroup of hydrocephalus patients referred for other reasons (34.3 cm) (Table 2). When cephalic perimeters of hydrocephalus sufferers were compared for two distinct periods (1987 to 1991 and 1992 to 1998), no significant difference was observed (p = 0.751) (Table 3).

### Table 2 - Means, standard deviations and medians of head circumference (HC) in the hydrocephaly cases referred with previous diagnosis and the hydrocephaly cases referred due to other reasons from 1987 to 1991 and from 1992 to 1998

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>37.7</td>
<td>34.3</td>
<td>34.8</td>
<td>36.5</td>
</tr>
<tr>
<td>Standard deviation</td>
<td>6.5</td>
<td>4.9</td>
<td>4.5</td>
<td>6.3</td>
</tr>
<tr>
<td>Median</td>
<td>37.0</td>
<td>34.0</td>
<td>35.5</td>
<td>35.0</td>
</tr>
</tbody>
</table>

The difference between the HC of the cases referred due to hydrocephaly and the other cases is significant (p = 0.0071)

### Table 3 - Percentiles of head circumference (HC) in the hydrocephaly cases referred with previous diagnosis, and in the cases referred due to other reasons, from 1987 to 1991 and from 1992 to 1998

<table>
<thead>
<tr>
<th></th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>&lt; 10</td>
<td>3 (5.4)</td>
<td>4 (13.3)</td>
<td>1 (6.3)</td>
<td>7 (9.2)</td>
</tr>
<tr>
<td>Normal</td>
<td>15 (26.7)</td>
<td>14 (46.7)</td>
<td>7 (43.7)</td>
<td>26 (34.2)</td>
</tr>
<tr>
<td>&gt; 90</td>
<td>38 (67.9)</td>
<td>12 (40.0)</td>
<td>8 (50.0)</td>
<td>43 (56.6)</td>
</tr>
</tbody>
</table>

The prevalence of HC > the 90th percentile in the cases referred due to hydrocephaly is significant (p = 0.034).

### Discussion

The CAISM, being a center of excellence, with a Fetal Medicine service active since 1993, presents a higher incidence of CD (5.7%) when compared with the incidence among the general population of 3%17 and with the general incidence of ECLAMC (2.7%).16 With respect to hydrocephalus patients, known global incidence is between 0.3 and 1.0/1,000 births.19-14 Within ECLAMC, during the period from 1982 to 1998 the recorded incidence of hydrocephalus was 0.74/1,000.16 This study detected an incidence of hydrocephalus almost five times greater - 3.16/1,000. Among these newborns a predominance was observed of cesarean deliveries (58.7%) and of premature births (average gestational age at birth of 36.6 weeks) with insufficient average birth weight (2,606 g). This data is compatible with a group of severe congenital defects, as is the case of hydrocephalus.

The ease of hydrocephalus detection using ultrasound scan is well known in the literature. Pober, Greene and Holmes, in a study of 59 fetuses with anomalies of the CNS associated or not with other anomalies, found a 90% level of accuracy for hydrocephalus patients, 33% for other anomalies of the CNS and 24% for extra-CNS anomalies.18 Nyberg et al. (1987), found 90% accuracy in the detection of hydrocephalus associated or not with other CNS anomalies.19

The increasing hydrocephalus tendency in CAISM, during the period studied, particularly from 1992 onwards, was noticeable both in the subgroup of previously referred cases with previous fetal diagnoses of hydrocephalus (68 cases - 66%), and among those cases referred for other reasons (35 cases - 34%). The tendency in the first group favors the interpretation of the direct and real influence of prenatal diagnosis upon the general incidence of hydrocephalus patients at the CAISM. This is corroborated by the fact that hydrocephalus is a structural anomaly which is easy to detect while still in the womb18,19 and, therefore, capable of directly influencing the incidence at birth of this defect since evaluation is made based on a population of hospital-born children, as is the case in this study.

Taking two other diagnoses for comparison - Down Syndrome (DS) and cleft lip and palate, both detectable during the prenatal period, although less frequently detected during this phase, at least in our environment, there is no observable increase in the incidence of these defects among the births at the CAISM during the same period. The frequency of prenatal diagnosis among the hydrocephalus patients was 85.5% while those with DS and patients with cleft lip and cleft palate were, respectively, 7.5% and 14.3%, (Figure 1). Despite the USS test nowadays being potentially available for all expectant mothers receiving prenatal care from the public health network, it is not always performed and, in the majority of cases, is only performed after the 1st trimester of gestation, when the evaluation of nuchal translucency, the main measurement used in tracking Down Syndrome is no longer possible.20 Cleft lips and palates, on the other hand, while detectable from the start of the second trimester onwards are rarely diagnosed as the fetal morphology exam is not routine in our locale.

The increasing tendency in the subgroup of hydrocephalus patients referred for other motives is more suggestive of a real increase in the incidence of hydrocephalus. However, among these cases, the following was observed: four were referred for other fetal defects and
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20 cases were referred because of maternal pathology, both situations in which the care given to expectant mothers is increased provoking an increased derivation of such patients to tertiary hospitals, in this case the CAISM and a contribution to this tendency.

When the incidence of hydrocephalus patients is analyzed by subgroup (isolated, associated with congenital infection, associated with dysmorphic syndromes and associated with other structural defects), only the isolated hydrocephalus subgroup presented a significant tendency to increase (Table 1). It would appear, at first glance, that a real increase in hydrocephalus was occurring, however it is appropriate to remember that isolated hydrocephalus patients form a highly heterogeneous group from the point of view of etiology, it would be more difficult to accept the hypothesis that a number of different etiological factors, all at the same time, were acting to cause an increase in the incidence of this anomaly. In all events, this analysis has enabled the ruling out of increases in incidences for relatively well defined groups, such as congenital infections and dysmorphic syndromes.

As was expected, this sample had a predominance of macrocephaly (55.4% of cases had cephalic perimeters >90th percentile). The average cephalic perimeter at birth and the predominance of cephalic perimeters greater than percentile 90, were greater in the group of hydrocephalus patients referred with a previous diagnosis, suggesting that the larger hydrocephalus, being more serious are detected earlier and are probably easier to diagnose before birth. The similarity of cephalic perimeters between the two periods analyzed (1987 to 1991 and 1992 to 1998), eliminates an initial hypothesis made by the authors that the increase in the incidence of hydrocephalus during the second period was directly associated with the detection of ventricular enlargement by prenatal ultrasound scan USS without increase in cephalic perimeter. Nevertheless it is interesting to note that of the 111 cases, 29 presented a normal cephalic perimeter and, in seven cases the perimeter was below the tenth percentile (Table 3). Therefore in the absence of prenatal USS 36 cases would not have been detected, since these cases did not present morphological alterations at birth. It is plausible therefore to suggest, that rather than a real increase in the incidence of hydrocephalus patients during the period studied, there was, in fact, under-diagnosis of hydrocephalus patients at birth before the increase in the use of ultrasound during the prenatal period. In other words, what today appears to be an increase in the incidence of hydrocephalus patients at birth, in reality is reflecting the under-diagnosis of this anomaly in the past.

In addition to the role that prenatal ultrasound tests played and to the characteristics of the CAISM, a university hospital and regional center of excellence, during the period studied certain events occurred with certainly contributed to some of the results found. The Perinatal Genetics program, run at the CAISM, started in 1993, has allowed better investigation of CD, increasing, for example the number of syndromes diagnosed, which without these investigations would have been referred to simply as presenting multiple malformations. The Fetal Medicine Service at the CAISM, also dating from 1993, has contributed, and continues to contribute to a rise in referrals of expectant mothers at high risk due to fetal reasons. These events favor greater attention to congenital defects and improved conditions for the diagnosis and treatment of more serious patient, as is the case of those with hydrocephalus.

References