Mental health at 5 years among children born extremely preterm: a national population-based study

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Abstract The objective of this study was to compare mental health at 5 years in children born extremely preterm with a reference group, and assess associations between functional abilities and mental health within the preterm group. In a national Norwegian cohort with gestational age 22–27 weeks or birthweight 500–999 g, mental health was assessed with the Strengths and Difficulties Questionnaire (SDQ), cognitive function with the Wechsler Preschool and Primary Scale of Intelligence-Revised (WPPSI-R), motor function with the Movement Assessment Battery for children (ABC-test) and severity of cerebral palsy (CP) with the Gross Motor Function Classification for CP (GMFCS). Neurodevelopmental disabilities (NDD) were described as mild and moderate/severe. SDQ of the preterm children was compared with that of an unselected reference group. SDQ sub-scores ≥90th percentile of the reference group were defined as a mental health problem and a Total Difficulties Score ≥90th percentile (TDS90) as suggestive of psychiatric disorder. Of 361 eligible preterm children, parents completed SDQ for 255 (71%). 97 (38%) had TDS90 compared to 116 (11%) of the reference group (OR 5.1; 95% CI 3.7–7.1). For the preterms, the rate of TDS90 was higher for those with moderate/severe NDD (27/37 vs. 27/116, adjusted OR 8.0; 95% CI 3.2–19, and mild NDD 43/102 [adjusted OR 2.2 (1.2–4.1)]. For preterms with no NDD, TDS90 was more common than for the reference group (27/116 vs. 116/1,089, OR 2.5; 95% CI 1.6–4.1). Extreme prematurity was associated with increased risk of later mental health problems, particularly if they had other functional impairments.

Keywords Extremely premature infant · Extremely low birthweight · SDQ · Mental health · Follow-up

Introduction

Children born preterm have been reported to be at increased risk of developing mental health problems, e.g. related to behaviour, inattention, hyperactivity and interaction with peers [1–4]. The rate appears to increase with decreasing gestational age (GA), while the characteristics of such difficulties do not change significantly with decreasing GA [5], although it has been suggested that attention deficit and hyperactivity disorder (ADHD) and mood disorders are more common among the most immature within the preterm group [6]. Mental health problems may also be associated with other factors, e.g. neurodevelopmental disability (NDD), gender and socioeconomic status (SES), and such factors are important to include when assessing the significance of prematurity per se [7–9].

The Strengths and Difficulties Questionnaire (SDQ) is a 25-item behavioural screening instrument which is widely used when assessing mental health in epidemiological studies of groups of children with or without chronic diseases [10–14]. The aims of the present study were to...
determine the prevalence and nature of mental health problems among children born extremely preterm compared with that of an unselected reference group of the same age using SDQ, and assess to what extent mental health problems among children born extremely preterm were associated with prematurity per se or with functional impairments related to being born preterm.

Materials and methods

Population

The study population was a national cohort of all children with gestational age (GA) <28 weeks or birthweight (BW) <1,000 g born in Norway in 1999 and 2000 which was prospectively followed from birth until 5 years of age. Major outcomes were known for all except two children until 2 years of age, and characteristics of the cohort, definitions and overall outcome in terms of mortality and morbidity until 5 years of age have been published [15–17].

The reference group was children born in 2001 attending the scheduled routine public health care program at 5–6 years of age in Oppland County, Norway. Oppland County is one of 20 counties in Norway, and its population is similar to that of Norway as a whole with respect to rural and urban residence. In Norway, a routine follow-up at this age, i.e. at school entry, is part of the national health care program for all children, and nearly 100% attend. All families were invited by local public health nurses to answer additional health-related questionnaires, including SDQ, as part of the follow-up.

Clinical examination

At 5 years the prematurely born children were examined at their local paediatric department according to the research protocol [17]. Independent of each other, a paediatrician performed a general clinical and neurological examination, a psychologist tested cognitive abilities with the Wechsler Preschool and Primary Scale of Intelligence-Revised (WPPSI-R) [18], and a physiotherapist assessed motor function with the Movement Assessment Battery for children (ABC-test) [19]. Reference mean for the full IQ (FIQ) score is 100 and one standard deviation (SD) is 15. The ABC-test consists of eight tasks in three major fields; manual dexterity, ball skills and balance (static and dynamic). Total age-specific scores range from 0 to 40, and increasing scores mean poorer function. A total score >95th percentile is classified as a motor problem. Gross motor function for children with cerebral palsy (CP) was classified according to the Gross Motor Function Classification for CP (GMFCS), which is a five-level classification. In short, class 1 means that the child is freely ambulatory, class 2 means inability to run or jump, class 3 means dependency on devices for walking, and classes 4 and 5 mean non-ambulatory CP [20]. Visual function and hearing were obtained from previous examinations. All children in Norway have a vision screen at four and pure tone audiometry at 5 years of age, and any significant deviation results in referral to an ophthalmologist or otolaryngologist.

Neurodevelopmental disability

Functional level has been described earlier and classified according to definitions used in the EPICure study [1, 17]: Severe NDD was defined as one or more of the following: CP class 4–5 on the GMFCS, FIQ more than 3 SD below the reference mean value of 100, i.e. <55 on the WPPSI-R, blindness or complete deafness. Moderate NDD was defined as CP class 2–3 on the GMFCS, FIQ 2–3 SD below mean, i.e. 55–70, severe visual impairment or need of hearing aid. Minor NDD was defined as CP class 1, FIQ 1–2 SD below mean, i.e. 70–84, ABC-test score >95th percentile, squint/refractive error or mild hearing loss. No NDD was defined as no CP, FIQ <1 SD below mean, i.e. ≥85, ABC-test score ≤95th percentile, and normal vision and hearing.

Mental health

The SDQ was completed by the parents. SDQ is a behavioural screening questionnaire for 4- to 16-year-old children [10]. The 25 items which describe positive and negative attributes of children can be allocated to five subscales with five items each: Emotional Problem Scale, i.e. symptoms such as fears, unhappiness and worries; Hyperactivity Problem Scale, i.e. symptoms such as restlessness, distractibility and fidgetiness; Conduct Problem Scale, i.e. symptoms such as tempers, fighting and stealing; Peer Problem Scale, i.e. peer-related problems such as being unpopular, bullied or solitary, and Prosocial Behaviour Scale, i.e. behaviour of being caring and helpful. For subscales other than the Prosocial Behaviour Scale, higher scores mean more problems. A Total Difficulties Score is computed by collapsing the first four subscale scores. Each item is scored on a three point scale; “not true”, “somewhat true” and “certainly true”, with total subscale scores ranging from 0 to 10 and Total Difficulties Score from 0 to 40. For each of the subscales a score at or above the 90th percentile of the reference children was defined as a mental health problem and a Total Difficulties Score at or above the 90th percentile (TDS90) was considered as a risk of having a psychiatric disorder as recommended by Goodman [21–23]. For the Prosocial Behaviour Scale a score less than the approximate 10th percentile of the reference group was considered a behaviour problem. Information on referral to
psychiatric care was obtained from questionnaires completed by parents.

Statistical analyses

First, the preterm and reference groups were compared with respect to mean SDQ sub-scales and Total Difficulties Score using t tests. Second, proportions of preterms with problem scores at or above the 90th percentiles and Prosocial Behaviour Scale score at or less than the 10th percentile of the reference group were calculated and differences presented as odds ratios (OR) with 95 % confidence intervals (CI) using the Chi-square test. Due to the stepwise change in SDQ scores, the exact 90th and 10th percentiles could not be defined and scores above an approximated 90th percentile (88th–93rd percentiles for the various sub-scales) and below an approximated 10th percentile (9th percentile) were used as references (see Table 2). Third, for the preterm group logistic regression analyses were performed with SDQ scores less than or at or above the approximated 90th or 10th percentiles (Prosocial Behaviour Scale) as outcome measure and GA, NDD, gender and maternal education as independent variables. Mother’s education was classified as high if she had completed at least 3 years of college or university education after high school; otherwise, it was classified as lower education.

SPSS statistical package version 15.0 was used for all analyses.

The study was approved by the Regional Committee on Medical Research Ethics and the Norwegian Data Inspectorate, and parents gave written informed consent.

Results

Population

Of 372 children born extremely preterm and still alive at 5 years of age, SDQ was completed for 255 (69 %, Fig. 1). One child was excluded due to Down syndrome, 65 children did not meet at the 5 year follow-up, 41 met for the follow-up, but their parents, for unknown reasons, did not complete the SDQ form, and parents of 10 children declined to complete the SDQ form because they felt it was irrelevant due to the severity of their child’s disability (six had severe cognitive impairment and CP level 5 on the GMFCS, three were blind or deaf in addition to other severe impairments and one was autistic). The mean age was 5 years and 10 months (SD 4 months). Exempting the 10 children with severe disability, there were no significant differences in early clinical characteristics between those who had the SDQ completed or not, although those assessed tended to be more immature (Table 1).

For the reference cohort, 1,119 of approximately 1,800 invited children (62 %) participated, and parents of 1,089 (97 %) completed the SDQ. Their mean age was 5 years and 9 month (SD 5 months). There were no difference between the children with completed SDQ and the rest of the cohort in terms of age, gender distribution, height or weight, which were the only parameters permitted to be collected for those who did not respond.

Children born preterm versus the reference group

The preterm children had higher mean scores on all problem subscales and “Total Difficulties Score” and a lower mean score on the “Prosocial Behaviour Scale” than the reference group (Table 2). Furthermore, 36–49 % had
scores above the approximate 90th percentiles for the reference group on the problem subscales, giving ORs in the range of 5.2–8.5 (highest for the hyperactivity and emotional problems scales), and 38 % (OR 5.2; CI 3.7–7.1) had a “Total Difficulties Score” above the 90th percentile (TDS90, Table 2). On the “Prosocial Behaviour Scale”, a slightly higher proportion of the prematurely born children scored less than the 10th percentile (Table 2). There were no significant gender differences in mean scores or proportions with scores in the range of mental health problems, neither within the preterm nor the reference groups, but for the preterm group there was a trend that boys more often had hyperactivity problems, conduct problems and TDS90 (OR 1.6; 0.9–2.7, OR 1.8; 0.9–3.5 and OR 1.3; 0.9–2.0, respectively). High maternal education was less common among the mothers of the preterm group (45 vs. 56 %, p = 0.002). When adjusting for mothers’ education and gender the rate of TDS90 was still increased for the children born preterm (OR 4.9; 95 % CI 3.5–6.8).

Preterm children with or without neurodevelopmental disabilities (NDD)

The rates of sub-scores above the 90th percentile and TDS90 were higher for the preterm children with severe or moderate NDD and also for those with minor NDD, compared to those with no NDD (TDS90 27/37 vs. 27/116, adjusted OR 8.0; 95 % CI 3.2–19, and 43/102 vs. 27/116, adjusted OR 2.2; 95 % CI 1.2–4.1) (Table 3).

Also, preterm children with no identified NDD more commonly had SDQ problem scores above the 90th percentile than the reference group, but there was no significant difference for the “Prosocial Behaviour Scale” (Table 4).

In a binary logistic regression analysis with TDS90 as the dependent variable and gender, mothers’ education, GA and NDD as independent variables significant predictors of a high score were NDD (OR 2.6; 95 % CI 1.8–3.8) and high maternal education (OR 0.4; 95 % CI 0.2–0.6).

Among the prematurely born children 19 (8 %) had been referred for child psychiatric follow-up compared to 10...
In this national cohort of 5-year-old children born extremely preterm, the rate of mental health problems expressed as scores at or above the 90th percentile on the SDQ problem scales was substantially higher than for an unselected reference group of similar age. Within the preterm group, the frequency of mental health problems increased with increasing severity of NDD, but even for the preterm children without identified NDD, i.e. almost half the preterm population, the rate of mental health problems was significantly higher than that for the reference population.

The strength of the present study was the national cohort design of the preterm group with detailed information on

Table 2
Mean scores and proportion with scores indicative of mental health problems (≥90th percentile except <10th percentile on the Total difficulties (TDS90) scale) on the Strengths and Difficulties Questionnaire (SDQ) for extremely preterm children born in Norway 1999–2000 (gestational age 22–27 weeks or birthweight 500–999 g) and a reference group at 5 years of age (children born in Oppland County, Norway, in 2001 attending the routine public health care program at 5–6 years of age)

<table>
<thead>
<tr>
<th></th>
<th>Preterms (n = 255)</th>
<th>Reference (n = 1,089)</th>
<th>Mean difference</th>
<th>95 % CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean SDQ scores</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emotional problem</td>
<td>2.3 (2.0)</td>
<td>1.2 (1.4)</td>
<td>−1.1</td>
<td>−1.3 to −0.9</td>
<td>0.0001</td>
</tr>
<tr>
<td>Hyperactivity problem</td>
<td>3.6 (2.7)</td>
<td>2.2 (1.9)</td>
<td>−1.4</td>
<td>−1.7 to −1.1</td>
<td>0.0001</td>
</tr>
<tr>
<td>Conduct problem</td>
<td>1.3 (1.5)</td>
<td>0.9 (1.1)</td>
<td>−0.4</td>
<td>−0.6 to −0.2</td>
<td>0.0001</td>
</tr>
<tr>
<td>Peer problems</td>
<td>1.5 (1.9)</td>
<td>0.7 (1.2)</td>
<td>−0.8</td>
<td>−1.0 to −0.6</td>
<td>0.0001</td>
</tr>
<tr>
<td>Prosocial behaviour</td>
<td>8.4 (1.6)</td>
<td>8.6 (1.4)</td>
<td>0.3</td>
<td>0.1 to 0.5</td>
<td>0.003</td>
</tr>
<tr>
<td>Total difficulties</td>
<td>8.7 (5.8)</td>
<td>5.0 (3.8)</td>
<td>−3.7</td>
<td>−4.3 to −3.1</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

Table 3
Number and proportions [proportions and odds ratio (OR) with 95 % confidence interval relative to no disability] with Strengths and Difficulties Questionnaire (SDQ) scores indicative of mental health problems (≥90th percentile except <10th percentile on the Total difficulties (TDS90) scale) according to severity of neurodevelopmental disabilities among 5 year old children born extremely preterm (gestational age 22–27 weeks or birthweight 500–999 g) in Norway in1999–2000

<table>
<thead>
<tr>
<th></th>
<th>No disabilitya</th>
<th>Minor disabilityb</th>
<th>Moderate or severe disabilityc</th>
<th>n (%)</th>
<th>n (%)</th>
<th>OR (total)</th>
<th>95 % CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Emotional problem</strong></td>
<td>32 (28)</td>
<td>50 (49)</td>
<td>2.5 (1.4–4.4)</td>
<td>17 (46)</td>
<td></td>
<td>2.2 (1.0–4.8)</td>
<td>2.0 (0.9–4.5)</td>
<td></td>
</tr>
<tr>
<td><strong>Hyperactivity problem</strong></td>
<td>34 (29)</td>
<td>59 (58)</td>
<td>3.3 (1.9–5.8)</td>
<td>31 (84)</td>
<td></td>
<td>12.5 (4.78–33)</td>
<td>12.2 (4.3–34)</td>
<td></td>
</tr>
<tr>
<td><strong>Conduct problem</strong></td>
<td>37 (32)</td>
<td>37 (36)</td>
<td>1.2 (0.7–2.1)</td>
<td>18 (49)</td>
<td></td>
<td>2.2 (1.04–4.8)</td>
<td>1.8 (0.8–4.0)</td>
<td></td>
</tr>
<tr>
<td><strong>Peer problem</strong></td>
<td>40 (35)</td>
<td>33 (32)</td>
<td>0.9 (0.5–1.6)</td>
<td>27 (73)</td>
<td></td>
<td>5.1 (2.3–12)</td>
<td>5.1 (2.2–11)</td>
<td></td>
</tr>
<tr>
<td><strong>Prosocial behaviour</strong></td>
<td>16 (9)</td>
<td>11 (11)</td>
<td>0.8 (0.3–1.7)</td>
<td>9 (24)</td>
<td></td>
<td>2.0 (0.8–5)</td>
<td>1.5 (0.7–3.1)</td>
<td></td>
</tr>
<tr>
<td><strong>Total difficulties</strong></td>
<td>27 (23)</td>
<td>43 (42)</td>
<td>2.4 (1.3–4.3)</td>
<td>27 (73)</td>
<td></td>
<td>8.9 (3.8–21)</td>
<td>8.0 (3.2–19)</td>
<td></td>
</tr>
</tbody>
</table>

- **a** No CP, FIQ ≥85, ABC score ≤95th percentile, and normal vision and hearing
- **b** CP class 1, FIQ 70–84, ABC score >95th percentile, squint/refractive error or mild hearing loss
- **c** CP >class 1, FIQ <70, severe visual impairment or need of hearing aid
- **d** Adjusted for mother’s education and gender

(1 %) of the reference group (OR 6.7; 95 % CI 3.0–15.0, p = 0.01). Forty preterm (16 %) versus 24 reference (2 %) children had either been referred to psychiatric follow-up or had TDS90 (OR 8.4; 95 % CI 5.0–15.0, p = 0.001).
all but two eligible subjects until 2 years of age, i.e. we are confident that the assessed group was representative for the whole cohort. Furthermore, they were assessed for functional abilities at the time when screened with SDQ. Assessment of mental health in children of preschool age using a screening questionnaire carries uncertainties, e.g. a Norwegian study suggested that the SDQ may identify a likelihood of a mental problem rather than a specific psychiatric disorder [22]. However, by including an unselected reference group the study provided an estimate of relative risk of mental health problems related to extreme prematurity [12, 13]. Weaknesses were that the response rate was relatively low among the reference group which may have resulted in a selection bias in favour of children without mental problems, and that information on general health and development for the reference group was based only on parents’ report and assessments by public health nurses and general practitioners at the public health care clinics.

The present study confirms previous reports that children born extremely preterm commonly have signs of mental health problems from early childhood [1–4, 8], and extends earlier studies by describing the nature of such problems and associations with functional abilities and social factors. The present results therefore indicate that this risk of mental problems increases with increasing NDD. This observation and the finding that the rate was higher also for children born extremely preterm without NDD than for an unselected reference population are important when advising parents, health personnel and teachers, and when designing follow-up and intervention programs for extremely premature infants. Eight percent of the preterm versus 1 % of the unselected reference children had been referred to child psychiatry prior to the 5-year assessment. However, as many as 16 % of preterm and 2 % of the reference children were either referred to child psychiatry or were at risk of psychiatric disorders as judged from TDS90 suggesting that it may be difficult to reveal a risk of psychiatric disorder at 5 years of age. This observation underscores the importance of examining predictivity of early development on future mental health and thus developing evidence-based follow-up programs.

The pattern of difference between the preterm and the unselected reference children with respect to the different SDQ subscales was similar for the total group of preterm children and for the preterm children without NDD, although less pronounced for the latter, suggesting that this pattern may be typical for survivors of extreme preterm births. It is noteworthy, however, that the prematurely born children with moderate or severe NDD differed from those without NDD in that they were more likely to have hyperactivity and peer-related problems indicating that these symptoms are more common among the preterm children with neurological impairments.

There was a non-significant trend that preterm boys more often had conduct and hyperactivity problems than preterm girls. This finding is similar to that of the EPICure study, but the differences were greater in the EPICure study, possibly because the children were more immature (GA <26 weeks) [8]. In the present population, we have previously described that the boys more often had lower IQ and poorer motor function than the girls [17]. Extremely preterm boys therefore appear to be at higher risk of cerebral dysfunction in most areas strengthening the hypothesis that the immature brain is more vulnerable in boys [24, 25].

Almost one in four of the preterm children without NDD had Total Difficulties Scores that are associated with risk of psychiatric disorders [11, 22, 23]. These children without a noticeable neurodevelopmental impairment may therefore struggle in everyday life to the extent that they may have a social handicap. The significance of addressing mental health issues was also demonstrated in the EPICure study [26]. Further studies are needed, however, to evaluate how well mental health screening at preschool age can predict later mental health and social function, and in order to design remedial programs.
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