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Fetal hemodynamics and language skills in primary school-aged children with fetal growth restriction: A longitudinal study

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ABSTRACT

Aim: Long-term follow-up studies on children born with fetal growth restriction (FGR) have revealed a specific profile of neurocognitive difficulties, including problems with speech, language and literacy skills. We hypothesized that problems with communication skills, including language use and literacy skills of FGR children at primary school age are associated with prenatal circulatory changes.

Methods: Ultrasonographic assessment of fetoplacental hemodynamics was performed prenatally in 77 fetuses. After a follow-up period of 8–10 years, assessment of reading and spelling skills using standardized tests and the Children's Communication Questionnaire (CCC-2) was performed to measure different language skills in 37 FGR children and 31 appropriately grown (AGA) controls, matched for gestational age.

Results: Increased blood flow resistance in the umbilical artery (UA PI > 2 SD) during fetal life showed odds ratios of 3.5–19.1 for poor literacy and communication skills and need for speech and language therapy. Furthermore, FGR children with prenatal cerebral vasodilatation (cerebroplacental ratio (CPR) < −2 SD) had significantly poorer literacy and communication skills, at primary school age compared to the AGA controls. Abnormal CPR demonstrated odds ratios of 4.2–28.1 for poor literacy and communication skills and need for speech and language therapy.

Conclusion: Increased blood flow resistance in the umbilical artery and cerebral vasodilatation are associated with poor communication, language, and literacy skills at early school age in children born with FGR. These findings indicate the need for continuous follow-up of this group and timely targeted support to ensure optimal academic outcomes.

1. Introduction

Fetal growth restriction (FGR) is associated with significant short-term and long-term mortality and morbidity [1,2]. Despite intensive research on FGR, the timing for delivery to ensure optimal long-term outcomes is still under evaluation. In clinical practice, the risks of prematurity are weighed against the deterioration of placental function and fetal distress by using fetal Doppler findings, biophysical profile score, and cardiotocography (CTG) in serial fetal surveillance tests. Placental insufficiency, the most common cause of FGR, may result in chronic fetal hypoxia [3], and as an adaptive mechanism to hypoxia, blood flow in the fetus is redistributed in favor of vital organs, the heart, and the brain [4–6]. Cerebral vasodilatation was earlier regarded as a protective autoregulatory mechanism and referred to as `brain sparing` [7,8], but recent findings suggest that cerebral redistribution, often assessed clinically using the cerebroplacental blood flow ratio, may not be entirely a protective phenomenon [9]. Adverse neonatal outcomes, reduced neonatal brain volumes, and increased risk for adverse neurocognitive outcomes in early childhood have been associated with fetal cerebral vasodilatation [10–14].

Development of sufficient language and communication skills is essential for a child's cognitive development and academic

Abbreviations: AGA, appropriate growth for gestational age; ARED, absent or reversed end-diastolic flow; CCC, children's communication checklist; CPR, cerebroplacental ratio; CTG, cardiotocography; FGR, fetal growth restriction; GCC, general communication composite score; MCA, middle cerebral artery; PI, pulsatility index; UA, umbilical artery

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performance. Indeed, reading and spelling skills are essential for reading comprehension and later academic and occupational success, and sufficient language and communication skills are needed in order to successfully use language in various situations and social contexts [15–18]. In particular, pragmatic language skills, which are defined as the appropriate use and interpretation of language in relation to the context in which it occurs, play a significant role in effective communication [19]. Previously, a detailed analysis of the FGR children included in this cohort have shown poor performance in reading and writing skills as well as in communication skills at primary school age [20,21], with a wide variation seen between the individuals. While detailed data concerning fetal circulatory changes and language skills at early school age are lacking, we wanted to evaluate data on communication and literacy skills of these FGR children [20,21] in relation to fetal hemodynamics.

In the present study, we hypothesized that poor communication and literacy skills of FGR children at primary school age are associated with fetoplacental hemodynamic changes. Specifically, we were interested in examining the impact of increased umbilical artery pulsatility and the balance between the cerebral and placental circulations on communication and literacy skills at primary school age.

2. Materials and methods

The study participants belonged to a prospectively collected cohort (n = 77) of growth-restricted fetuses (birth weight < 10th percentile and/or umbilical artery (UA) pulsatility index > 2 SD in a normal population [22,23]. The mothers were recruited in 1998–2001 from our high-risk prenatal unit, and were later contacted to book a follow-up visit in accordance with the protocol when their children reached 8–10 years of age (Fig. 1). In all cases, gestational age was confirmed by ultrasound before 20 gestational weeks. Pregnancies with major structural and chromosomal abnormalities, and those complicated by chorioamnionitis and/or ruptured membranes were excluded. From the originally collected cohort, 39 children attended the follow-up visit. Two children were excluded from the analyses because of the child's unwillingness to perform the tests (n = 1) and insufficient Finnish language skills (n = 1). The control group consisted of 31 children with appropriate growth for gestational age (AGA) (birth weight > 10th percentile). The control group was selected from delivery room records and these children were matched for gestational age, gender, mode of delivery and delivery within ± 2 weeks of the index FGR neonate. The research protocol was approved by the Ethical Committee of the Oulu University Hospital (approval number 8/2008 on February 21, 2008). Study participation required written maternal consent.

2.1. Prenatal assessment

Maternal characteristics and obstetric data were collected at the study entry. Maternal hypertensive disorders were categorized according to the guidelines of the American College of Obstetrics and Gynecology [24] and prenatal steroid therapy included two 12 mg betamethasone doses at 24 h apart.

Detailed information concerning placental and fetal hemodynamic assessments collected by a single investigator within a week (median of 2.9 days) prior to delivery has been described earlier [25]. Acuson Sequoia 512 (Acuson, Mountain View, CA, USA) with 4–8 MHz transducers were used for scanning, and the angle of insonation was maintained at < 15 degrees in all examinations. Three consecutive cardiac cycles were obtained and the mean values were used in the analyses. The pulsatility index (PI) in the UA was measured from the free loop of the umbilical cord and further categorized as normal, increased (UA PI > 2 SD), or absent/reversed end-diastolic (ARED) flow [23,26]. The middle cerebral artery (MCA) PI was assessed, and the cerebroplacental ratio (CPR) was calculated as the MCA PI/UA PI [27]. Significant placental insufficiency (UA PI > 2 SD) and redistribution of blood flow (CPR < −2 SD) were determined according to earlier published data [28,29].

The managing obstetrician was blinded to the study data. During 1998–2001, the indications for delivery were 1) worsening maternal condition, 2) abnormal non-stress test in fetal heart rate monitoring, and 3) abnormal pulsatility in the ductus venosus.

2.2. Postnatal outcomes

At birth the mode of delivery, UA blood gas values, Apgar scores, and neonatal morphometric measurements were recorded. The cohort children attended follow-up studies at the mean age of 9.2 years (Table 1). Follow-up studies included evaluations of speech, language, and literacy skills by a licensed speech therapist (LP). The children's medical charts were reviewed for diagnoses and data from questionnaires completed by the parents were collected. The questionnaires were created specifically for this study and included sections concerning diagnoses and frequent need for intensive preventive measures such as speech and language therapy, physiotherapy, occupational therapy, and special education. Socioeconomic characteristics were also

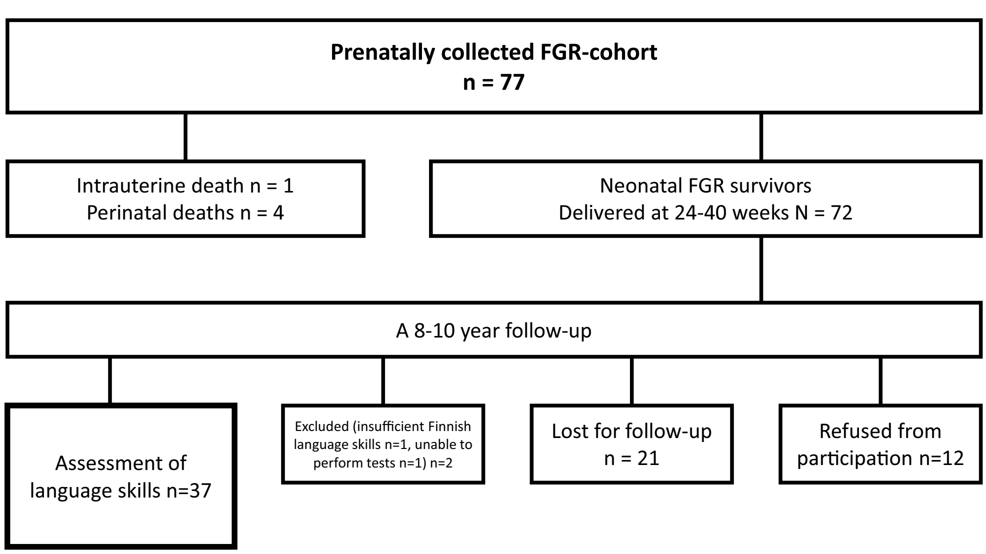

Fig. 1. Flow chart of the collected FGR cohort.

Table 1
Characteristics of 8–10-year-old children born with fetal growth restriction (FGR) and control children born with appropriate growth (AGA). Values are presented as median (range), mean (SD) and % (n).

	FGR $n = 37$	AGA $n = 31$	p-value
Maternal factors			
Age at delivery (years)	30 (17–41)	31 (20–42)	0.55
Maternal pre-eclampsia	41 (15/37)	3 (1/31)	< 0.001
Maternal education			
University	62 (23/37)	50 (15/30)	0.34
Vocational/basic education	38 (14/37)	50 (15/30)	
Prenatal factors			
Umbilical artery ARED	22 (8/37)	0	
Umbilical artery PI > 2 SD	68 (25/37)	0	
Middle cerebral artery PI < −2 SD	27 (10/31)	0	
Cerebroplacental ratio < -2SD	61 (19/31)	0	
Birth			
Gestational age (weeks)	35 (24–40)	35 (26–40)	0.97
Birth weight (g)	1750 (370–2940)	2490 (815–5190)	0.004
Male gender	43 (16/37)	42 (13/31)	1.00
5-minute Apgar < 7	15 (5/33)	0 (0/28)	< 0.001
Umbilical artery pH	7.28 (0.06)	7.26 (0.05)	0.28
Cesarean delivery	68 (25/37)	83 (24/29)	0.26
Postnatal factors			
Respiratory distress syndrome	28 (10/36)	26 (8/31)	1.00
Bronchopulmonary dysplasia	17 (6/36)	3 (1/31)	0.11
Intraventricular hemorrhage	6 (2/36)	10 (3/31)	0.66
Necrotizing enterocolitis	3 (1/35)	0 (0/31)	1.00
Retinopathy of prematurity	9 (3/35)	7 (2/31)	1.00
Hearing impairment	3 (1/37)	3 (1/31)	1.00
Speech and language therapy	60 (22/37)	32 (10/31)	0.03
Physio/occupational therapy	32 (12/37)	32 (10/31)	1.00
Attending mainstream education	70 (26/37)	97 (30/31)	0.008
Demographic factors			
Age at testing (years)	9.2 (0.4)	9.0 (0.2)	0.77
Weight (kg)	27.7(5.4)	30.9 (7.2)	0.02
Height (cm)	131.8 (6.0)	135.4 (7.3)	0.10
Head circumference (cm)	52.3 (1.9)	53.3 (1.3)	0.02
Family background			
Two parent family	95 (35/37)	87 (28/31)	0.54
Single parent family	2.7 (1/37)	6.5 (2/31)	
Other	2.7 (1/37)	6.5 (2/31)	
Speech/language/learning problems of siblings	22 (8/36)	30 (9/30)	0.48

ARED, absence or reversed end-diastolic flow; PI, pulsatility index.

recorded [30].

2.3. Assessments of communication and literacy skills

Communication and literacy skills were assessed with standardized methods at the mean age of 9.2 years (Table 1) as described in detail in our earlier studies (20, 21). The Children's Communication Checklist-2 (CCC-2) [31] identifies children with speech, language, and pragmatic language impairment as well as children requiring further assessment of autism spectrum disorder. A Finnish version of the CCC-2 questionnaire [32,33] for 8–10-year-old children was completed by the parents after brief verbal instructions. The General communication composite score (GCC) was calculated by summing the CCC-2 subscales from A to H; low scores (< 69 points according to the Finnish norms) indicated impaired communication skills [31,34] (Table 2). Reading and spelling skills, reading fluency, reading accuracy, and reading comprehension were evaluated by standardized Finnish tests (the Word Chain test [35], the Ytte test [36], the Lukilasse test [37]. Performance below the 10th percentile of the normal population was considered poor.

In clinical practice, detailed examinations and speech and language therapy are commonly recommended when problems in several areas of reading, spelling, and communication are identified. In the present study, speech and language therapy was indicated if a child performed below the 10th percentile normal value in > 50% of reading and spelling skill subtests and/or in the presence of a compromised (< 15th percentile normal value) score in the GCC.

2.4. Statistical analyses

The data were analyzed using the SPSS 22.0 for Windows software package (SPSS Inc., Chicago, IL, USA). The primary outcome measures were poor performance in communication skills (CCC-2), measured by the general communication composite (GCC), poor performance (< 10th percentile of normal population) in literacy skills, measured by comprehensive reading and spelling skills testing, and clinically estimated need for speech and language therapy. Demographic and ultrasonographic variables were analyzed for association with the primary outcome measures using logistic regression analysis. To estimate the OR in the presence of complete quasi separation, we used the brglm package [38] in the R program, version 3.4.2 [39]. The brglm package is based on the method for bias reduction [40] and allows estimation of the OR from sparse data.

Categorical data were compared using Chi-square analysis and the Fisher's exact test. For continuous variables, the Student's *t*-test was used if the data were normally distributed, otherwise the Mann-Whitney *U* test was chosen. Data are present as mean (SD), median (range), n (%), and odds ratio (95% confidence interval [CI]). A two-tailed *p*-value of < 0.05 was selected as the level of statistical significance.

3. Results

The characteristics of the FGR and AGA groups are presented in Table 1. Mothers of the FGR children demonstrated preeclampsia more frequently. There were 19% twins (7/37) in the FGR group and 23% (7/31) twins in the control group. In the FGR group, 68% had UA PI value > 2 SD, 22% (8/37) demonstrated ARED in UA, 27% showed MCA PI < −2 SD), and 61% had CPR < −2 SD. The Doppler parameters (UA PI, CPR) did not differ between the singletons and twins in the FGR group. This cohort was delivered at 24–40 gestational weeks with no differences in gestational age at delivery between the groups, neither did gestational age between the FGR subgroups (FGR UA PI > 2 SD, FGR CPR < −2SD and FGR MCA PI < −2 SD) and the AGA group differ. The Cesarean delivery rate was 68% and 83% in the FGR and AGA groups, respectively. In the mode-of-delivery matched AGA group, the indications for operative delivery were related to maternal fear of child birth and fetal presentation, while in the FGR group fetal distress was the most common indication. The FGR neonates had lower birth weights than the AGA group as expected. Although no significant differences were detected in UA pH values at birth between the groups, FGR children demonstrated low 5-minute Apgar scores (< 7) more frequently than the AGA group. However, the number of severe neonatal complications did not differ significantly between the groups.

Prior to the study assessment at the age of 8–10 years, the FGR children had received speech and language therapy more frequently than the AGA children. This was due to poor language skills (10 children vs. 2 children) and articulation problems (12 children vs. 8 children, Table 1), respectively. A total of 70% of the FGR children and 97% of the AGA children were studying in mainstream education. One FGR child was in a special education class and nine were receiving assistance in mainstream education, while only one AGA child required assistance in mainstream education classes (Table 1).

Seven (19%) FGR children performed below the 10th percentile normal values in all three literacy subtests (Ytte test, Word Chain test, Lukilasse test). Ten (27%) FGR children and four (13%) AGA children performed below the 10th percentile GCC normal value. According to a speech therapist's evaluation, 15 (41%) FGR children and five (16%)

Table 2
Short descriptions of the Children's Communication Checklist-2 (CCC-2) subscales. The General communication composite score (GCC) was calculated by summing the CCC-2 subscales from A to H. The questionnaires and scores related to CCC-2 and GCC are described in detail in our earlier publication [20].

CCC-2 subscales	Examples of the content of the subscales
Language structure	
A. Speech	Ability to pronounce clearly, at a normal rate and fluency of speech
B. Syntax	Ability to use grammar and long and syntactically varying utterances appropriately
C. Semantics	Ability to understand different meanings of the words and phrases
D. Coherence	Ability to tell about past and future events logically
Language use/pragmatics	
E. Inappropriate initiation	Tendency to talk to anyone/everyone and about things that everybody already knows/nobody is interested in
F. Stereotyped language	Tendency to change topics in conversation to one's own favorites and overuse favorite phrases
G. Use of context	Ability to comprehend and express utterances in different contexts relevantly
H. Non-verbal communication	Ability to use non-verbal communication like eye contact, facial expressions and gestures appropriately
Social behavior	
I. Social relationships	Ability to communicate appropriately with peers and adults
J. Interests	Tendency to focus strongly on one's own specific interests

Modified from Väisänen et al. *2014* [53].

AGA children were defined as being in need of speech and language therapy due to compromised performance in literacy skills, communication skills, or both. There were no differences in the follow-up results between singletons and twins, neither in the FGR group nor in the AGA group.

The FGR children with prenatal UA PI values of > 2 SD performed below the 10th percentile normal values in literacy skills significantly more often than AGA controls (Table 3). Communication skill testing using the CCC-2 revealed no statistically significant differences between FGR and AGA children in this cohort, but a more frequent need for speech and language therapy was detected among FGR children with UA PI > 2 SD compared to AGA controls (Table 3).

FGR children with significant blood redistribution (CPR < −2 SD) performed significantly more frequently below the 10th percentile normal values in literacy skills, demonstrated significantly poorer communication skills, and also needed speech and language therapy more frequently than the AGA controls (Table 3). At early school age, FGR children with CPR < −2SD had significantly smaller mean (SD) head circumference (52.0 (1.7) cm) compared to the AGA controls (53.0 (1.1) cm, $p = 0.01$). There were no significant weight and height differences between these subgroups.

In the presence of UA PI > 2 SD and adjusted for gestational age, the odds ratios for poor literacy skills, poor communication skills, and the need for speech and language therapy ranged between 3.5 and 19.1 (Table 4). The odds ratio for poor literacy skills was about 28-fold among FGR children with cerebral vasodilatation (CPR < −2 SD) compared to AGA controls, and a 4.2–5.0 times higher risk for impaired communication skills and a need for speech and language therapy was detected in this group compared to AGA children (Table 4).

4. Discussion

In the present study, FGR children with significant placental insufficiency and blood flow redistribution in favor of cerebral circulation demonstrated odds ratios of 4.2–28.1 for poor performance in literacy and communication skills and a need for further speech and language therapy. This indicates that placental insufficiency and low CPR during fetal life are associated with a risk of language and communication problems at early school age.

In previous studies, significant placental insufficiency with absent end-diastolic umbilical artery velocity has been associated with adverse neurocognitive outcomes in early childhood and at early school age [13,30,41]. In the prospective multicenter PORTO study investigating the impact of brain-sparing on FGR outcomes, the presence of both UA PI > 95th percentile of normal values and abnormal CPR increased the risk of adverse perinatal outcomes [11]. While all FGR children in our study except one with UA PI > 2 SD also had abnormal CPR, we are unable to ubiquitously speculate the impact of a sole UA finding on the outcomes.

About 53% of the FGR children who demonstrated CPR < −2 SD in our study were evaluated as needing speech and language therapy, and one third of these children also showed poor performance in literacy skills. Fetal cerebral vasodilatation, an indicator of fetal blood flow redistribution, seems to be associated with adverse short-term and long-term neurocognitive outcomes in FGR children with normal and increased UA pulsatility, although this has previously been considered as a benign adaptive mechanism [10,11,13,14,42,43]. Moreover, in neonates born prior to 32 weeks, Figueras et al. [10] reported an association between cerebral vasodilation and short-term neurobehavioral outcomes as measured by the Neonatal Behavioral Assessment Scale (NBAS), while the large randomized TRUFFLE trial detected no significant association between fetal cerebral vasodilatation and 2-year neurodevelopmental outcomes [10,44]. In the TRUFFLE trial, motor and perception deficits were included in the assessment of impaired neurodevelopment, which was determined as low Bayley Scales mental development score, estimated cognitive delay > 3 months, cerebral palsy, or severe hearing or visual impairment [44]. The authors of the TRUFFLE study concluded that fetal cerebral vasodilatation offered no

Table 3
Poor performance in communication and literacy skills in FGR children with abnormal umbilical artery flow (UA PI > 2SD), FGR children with cerebroplacental ratio below < −2 SD normal values (FGR CPR < -2SD) and AGA controls. The values are presented in % (n).

	AGA	FGR UA PI > 2 SD	FGR CPR < -2SD	p*	p **
Communication skills (CCC2) < 10th percentile normal value	13 (4/31)	36 (9/25)	42 (8/19)	0.06	0.04
Literacy skills < 10th percentile normal value	0 (0/31)	24 (6/25)	32 (6/19)	0.005	0.002
Clinically evaluated need for therapy	16 (5/31)	44 (11/25)	53 (10/19)	0.04	0.01

p* FGR UA PI > 2 SD vs AGA.
p** FGR CPR < -2SD vs AGA.

Table 4
Odds ratios (95% CI) for adverse outcomes in communication and literacy skills and need for speech and language therapy in FGR children with abnormal umbilical artery flow (UA PI > 2SD) (n = 25) and in FGR children with cerebroplacental ratio < -2SD (n = 19). The results are adjusted for gestational age.

	Communication skills (CCC2) < 10th percentile normal value	p	Literacy skills < 10th percentile normal value	p	Clinically evaluated need for therapy	p
AGA	Reference					
UA PI > 2 SD	3.5 (1.0–17.3.)	0.06	19.1 (2.1–∞)	0.04	3.9 (1.2–17.9)	0.03
CPR < - 2 SD	4.2 (1.1–21.1)	0.04	28.1 (∞–∞)*	0.02	5.0 (1.4–23.6)	0.02

* In the brglm-package of the R program, fit generalized linear models with binomial response use an adjusted-score approach to bias reduction. These procedures return estimates with improved frequentist properties (bias, mean squared error) that are always finite even in cases where the maximum likelihood estimates are infinite (data separation). Fitting takes place by fitting generalized linear models on iteratively updated pseudo-data.

advantages over birth weight and gestational age in the timing of delivery in FGR pregnancies prior to 32 weeks. However, fetuses with cerebral vasodilatation (abnormal umbilicocerebral ratio Z-score) at the time of the TRUFFLE trial entry, had a higher risk for poor 2-year neurodevelopmental outcomes [44]. Our study cohort included FGR fetuses born at a wide gestational age range (24–40 weeks), including 10 FGR children born prior to 32 weeks. A total of 88% of the preterm born FGR children demonstrated an abnormal CPR prenatally and 60% of them had problems in language and communication skills, while only 30% of AGA children born prior to 32 weeks showed impairment in these areas. We speculate that the differences are due to different study populations, study designs, and follow-up times.

Over 40% of the FGR children, who demonstrated cerebral vasodilatation (CPR < −2SD) prenatally, presented clinically significant impairment of communicative functions in our study (Table 3). Cerebral vasodilatation, a response to fetal hypoxemia, has been associated with compromised outcomes especially in the areas of communication and executive functions, which depend highly on frontal brain area function [14]. It has been speculated that frontal areas may be exceptionally susceptible even to mild hypoxia [42]. The second half of the pregnancy is essential as regards to formation of critical neuronal connections and myelination of important tracts, and during the third trimester, development of the cortical layers of the brain is accelerated making these parts especially vulnerable to adverse events [45]. Moreover, reduced gray matter volumes, which correlate with suboptimal neurodevelopment, and widespread microstructural changes in white matter have been detected in preterm FGR infants [46–48].

The catch-up growth of FGR children during the early years may have an impact on neurocognitive outcomes. In the large EPIPAGE study, postnatal catch-up growth did not affect neurocognitive outcomes at 5 years of age in children born with FGR [49], but Geva et al. (2006) reported compromised neurocognitive outcomes at 9 years of age in FGR children with poor postnatal head growth [50]. In a recent study on FGR children with prenatal cerebral blood flow redistribution, poor neurocognitive outcomes were associated with incomplete head circumference catch-up growth at 6 years of age [51]. Similarly, in our study, FGR children with cerebral redistribution had significantly smaller head circumferences compared with FGR children without cerebral redistribution, and AGA controls.

The CCC-2 questionnaire has been demonstrated to correctly identify impairments in language and pragmatic language use [34,52,53]. However, although the GCC is a validated method for identifying those children with clinically marked communication problems from the normal ones, it doesn't differentiate the type of problem very well [31]. In the present study, all children who scored below the 10th percentile in GCC had low scores (< the 10th percentile of normal values) in more than four subscales of the CCC-2, indicating clinically significant problems in communication skills. Problems in the development of language skills, especially pragmatic language skills, are associated with compromised general intellectual function and behavioral problems [18].

The literacy tests used in the present study are standardized tests that measure different aspects of reading and spelling. These skills are essential for a child to be able to obtain a sufficient level of reading comprehension [15,17]. Poor performance in all or most of the subtests indicates that a child has marked difficulties in reading and writing, and without support he will most likely also have difficulties in academic performance. Furthermore, difficulties in these areas have proved to be very persistent, indicating that children with poor skills at early school age will most likely have poor skills also in adolescence [54]. In previous studies concerning reading skills in preterm born children, difficulties have been shown to increase with advancing age [55]. Despite our national screening program, conducted prior to school entry as regards to speech and language therapy needs and more frequent speech therapy sessions in the FGR group compared to the AGA group, FGR children showed significant impairments in their linguistic performance. Our results, thus, underline the importance of continuous follow-up and targeted preventive measures in the FGR children, especially those with placental insufficiency and cerebral vasodilatation.

We recognize that the rather small sample-size is a limitation of our study. However, the children studied belong to a well-defined population-based cohort of growth-restricted fetuses. The children lost to follow-up/refusing to participate did not differ from the participants as regards to pre- or perinatal factors (data not shown). Our cohort includes children born at a wide range of gestational ages, but when FGR children were compared to their gestational age matched AGA peers, prenatal circulatory changes have been demonstrated to be a significant risk factor for adverse neurodevelopmental outcomes independent of gestational age [30,41]. We feel that long-term follow-up and a detailed linguistic and literacy assessment of FGR children in our cohort combined with prenatal hemodynamic evaluation is a significant strength of this study, while previously linguistic skills have been investigated mostly as a part of cognitive assessment [51,56,57].

5. Conclusion

We conclude that in FGR, increased umbilical artery pulsatility and cerebral vasodilatation are associated with poor communication and literacy skills at early school age, suggesting that these fetal circulatory changes play a significant role in the prediction of later communication and literacy problems. Therefore, preventive measures should be targeted in these FGR children to support the development of their academic abilities.

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Declaration of Competing Interest

The authors declare no conflicts of interest.

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