A prospective study of perinatal and metabolic risk factors for early childhood caries

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INTRODUCTION

Early childhood caries (ECC) is defined as the presence of one or more decayed tooth in a child under 6 years of age. Over 560 million children are affected worldwide, causing difficulties in sleeping, eating and attending school due to loss of tooth substance and pain. Classified as a non-communicable disease, ECC is thought to share socioeconomic, behavioural, biological and perinatal risk factors with other lifestyle-related conditions in childhood. Consequently, several attempts have been made in different populations to reveal associations between ECC and preterm birth, gestational age and body weight, but these studies have shown conflicting results. For example, an increased level of ECC in preterm children was demonstrated in a large cohort of...
Brazilian children,\(^3\) while a Japanese study failed to detect such a relationship.\(^4\) A Swedish study reported enamel defects but not caries to be more common in extremely preterm infants compared with age- and gender-matched full-term controls.\(^5\) However, recent data from longitudinal investigations have suggested that low birthweight may be associated with the development of caries.\(^6,7\)

The link between ECC and BMI has recently been addressed in a systematic review.\(^8\) The result was inconsistent, but the meta-analysis based on 12 studies suggested that overweight and obese children were at greater risk of having ECC. Given the current controversies concerning perinatal and metabolic risk factors for ECC, there is a need for further research relying on well-documented birth cohorts rather than cross-sectional or case-control studies based on retrospective data.

Our research group has previously investigated the mode of delivery and selected family characteristics in relation to the development of ECC.\(^9\) We have also shown that moderately preterm preschool children have an increased waist circumference\(^10\) and that the metabolic syndrome may be present even in preschool children.\(^11\) In the current study, we explore the possible associations between early childhood caries and preterm birth, birthweight, childhood weight status and metabolic risk factors in a cohort of children that was followed from birth up to 6.5 years of age.

## 2 | PATIENTS AND METHODS

### 2.1 | Study group

The participants were 208 children (105 boys and 103 girls) in a dental study subgroup of the endocrine cohort within the Halland Health and Growth study.\(^12\) This endocrine cohort comprised 551 children born with a gestational age ranging from 32 to 43 weeks at the Halland Hospital Halmstad, located in southwest Sweden.\(^9\) Pregnant mothers received written information about the study when visiting maternal healthcare units during the last trimester and gave consent to participation upon arrival at the delivery unit at the hospital. We recalled the children for endocrine follow-ups at five predetermined time points, ending at 6.5 years. Children delivered by caesarean section were recruited separately to enable other research questions and analyses to be conducted within the project. Therefore, the endocrine cohort included 78 children (37.5%) delivered by caesarean section and by that cannot claim of being population-based. At the age of 5 years, all children in the cohort were invited to a dental examination at the Maxillofacial Unit, Halland Hospital Halmstad, and the parents of 292 children accepted this offer. The analysis reported here is based on the 208 children who had a complete set of dental and perinatal data together with a successful metabolic examination at the age of 6.5 years. The most common reasons for dropping out from the metabolic examination were lack of cooperation and the child being in a non-fasting condition. A flow chart is given in Figure 1.

### 2.2 | Perinatal factors

Perinatal parameters such as gestational age, weight, length and head circumference were extracted from the medical records. We defined moderate-to-late preterm birth as a gestational age of 32-36 weeks. Infants were defined as appropriate for gestational age if their birthweight and length fell within plus or minus two standard deviation (SD) scores; infants below minus two SD scores were defined as small for gestational age and those above two SD scores were defined as large for gestational age.\(^13\) We collected maternal characteristics such as age at parturition, weight, length, smoking habits, educational level and employment from the medical records and through questionnaires.

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**FIGURE 1** A flow chart of subjects. The endocrine cohort (\(n = 551\)) consisted of 395 infants from the original Halland Health and Growth study, delivered vaginally or by caesarean section, that was merged with 156 infants exclusively delivered by caesarean section (the Caesarean section group). Of these, 292 took part in a dental examination, and fasting blood samples at the age of 6.5 y were available from 208 children.
2.3 | Metabolic examination

At 6.5 years of age, the children were examined by one of two trained research nurses. The children were weighed in their underwear on electronic step scales, and their height was measured with a stadiometer. Body mass index (BMI) was calculated as kg/m², and waist circumference was measured midway between the iliac crest and lowest rib after gentle expiration. We used age- and gender-specific cut-off values for waist circumference according to the IDEFICS monitoring level: ≥58.0 cm for girls and ≥58.5 cm for boys. Thereafter, blood pressure was measured and fasting blood samples were collected for analyses of cholesterol, triglycerides, high-density lipoprotein, low-density lipoprotein, glucose, insulin, HbA₁c and homeostatic model assessment for IR. Cut-off values for the metabolic syndrome (insulin resistance, high blood lipids and high blood pressure) were adopted from previous IDEFICS publications. We defined overweight and obesity according to Cole and Lobstein.

2.4 | Dental examination

Dental examination was performed in a fully equipped paediatric dental office by one of two experienced and calibrated examiners. Manifest caries (cavitated lesions) were registered according to the WHO criteria, and early, non-cavitated lesions were defined as a carious opacity or visual colour change (white or brown) of the enamel, with a rough surface. Caries prevalence was expressed as the presence of at least one early or cavitated lesion, and caries frequency was expressed as the sum of decayed, missing and filled teeth. Bitewing radiographs were taken to aid caries detection based on individual need. The two examiners assessed 10 preschool children independently prior to the study, and the inter-examiner agreement was 90%.

2.5 | Laboratory methods

The collected blood samples were immediately centrifuged, and the serum was frozen and stored at ~80°C until further analysis. Total cholesterol, triglycerides, high-density lipoprotein (HDL) cholesterol and low-density lipoprotein (LDL) cholesterol were measured by an enzymatic colorimetric assay on a Cobas 6000 analyser (Roche Diagnostics, GmbH). The intra-assay coefficient of variation was 1.9%, 1.8%, 1.0% and 0.7%, respectively. Glucose was determined by an enzymatic method with hexokinase and insulin, measured by an electrochemiluminescence immunoassay, both on the Cobas 6000 analyser. The intra-assay coefficient of variation was 2.2% for glucose and 2.0% for insulin.

2.6 | Statistical methods

The data were processed with the IBM SPSS software (version 25.0, IBM Corp.). We used descriptive statistics for normally distributed data and Student’s t test or a chi-square test to compare the dental study group and the endocrine cohort. Chi-square test with Fisher’s exact test was applied to calculate relative risk and Spearman’s rank correlation coefficient for the correlation analyses. All tests were two-tailed, and we considered a P-value < .05 to be statistically significant.

3 | RESULTS

3.1 | Demographics

The background characteristics of the dental study group and the endocrine cohort are shown in Table 1. The groups did not differ significantly with respect to the perinatal data. In the dental group, 6.3% were moderately to late preterm, 11.6% were born small for gestational age, and 4.8% were born large for gestational age. There were, however, some significant differences between the dental group and the endocrine cohort concerning the maternal background factors; the mothers in the dental group were older (P < .05), smoked less (P < .05) and had a higher educational level.

| Variable                     | Dental study group n = 208 | Endocrine cohort n = 551 | P-value |
|------------------------------|----------------------------|--------------------------|---------|
| **Perinatal data**           |                            |                          |         |
| Gestational age, d           | 277.6 (12.5)               | 279.1 (11.4)             | NS      |
| Birthweight, gram            | 3499 (621)                 | 3569 (604)               | NS      |
| Birth length, cm             | 50.4 (4.7)                 | 50.8 (2.4)               | NS      |
| Head circumference at birth, cm | 34.9 (1.6)                | 35.0 (1.7)               | NS      |
| SGA (%)                      | 11.6%                      | 9.8%                     | NS      |
| AGA (%)                      | 83.6%                      | 85.5%                    | NS      |
| LGA (%)                      | 4.8%                       | 4.7%                     | NS      |
| **Maternal data**            |                            |                          |         |
| Age, y                       | 31.8 (4.8)                 | 30.4 (5.1)               | <.05    |
| BMI, kg/m²                   | 24.6 (4.7)                 | 24.2 (4.4)               | NS      |
| Weight, kg                   | 68.6 (15.9)                | 68.4 (13.1)              | NS      |
| University educated (%)      | 70.2%                      | 59.3%                    | <.05    |
| Smoker (%)                   | 2.1%                       | 6.2%                     | <.05    |
| Unemployed (%)               | 2.7%                       | 5.0%                     | NS      |
| Born outside Sweden (%)      | 5.4%                       | 10.8%                    | <.05    |

Note: Values in the table denote mean (standard deviation) or per cent. Abbreviations: AGA, appropriate for gestational age; LGA, large for gestational age; NS, Not significant; SGA, small for gestational age.
level (P < .05). Furthermore, 5.4% were born outside Sweden in the dental group, compared with 10.8% in the endocrine cohort (P < .05).

### 3.2 | Associations between ECC, preterm birth and gestational age

The prevalence of ECC in the dental group was 17.8% with a mean caries frequency (decayed, missing and filled teeth) of 0.63. The relative risk for ECC in preterm infants and those born small or large for gestational age is shown in Table 2. Moderate-to-late preterm infants displayed a significantly higher caries prevalence compared with the full-term children (P < .05). Similarly, infants born small for gestational age showed an increased prevalence of caries compared to children born appropriate for gestational age (P < .05). A similar but statistically non-significant tendency (P = .054) was noted for infants born large for gestational age.

### 3.3 | Associations between ECC, BMI and metabolic risk factors

Of the 208 children in the dental group, 12.0% were overweight and 3.4% were obese at 6.5 years, but body weight was unrelated to the prevalence of ECC. One in five children (19.7%) had one risk factor for the metabolic syndrome according to the IDEFICS monitoring level, 13.9% had two risk factors, and 13.4% had three or more risk factors. We found no significant correlations between ECC and any of the recorded risk factors of the metabolic syndrome. Neither smoking habit, lack of maternal education nor unemployment was found to influence the risk to develop caries. A statistically significant correlation was found, however, between caries frequency and fasting blood glucose (r = 0.18; P < .05). The mean fasting blood glucose values also differed slightly between children with and without caries (4.8 (SD 0.4) vs 4.6 (SD 0.4) mmol/L; P = .05).

### 4 | DISCUSSION

The main finding of this study was that moderately to late preterm children displayed a significantly increased risk of developing early childhood caries, thereby confirming several previous observations.3,19,20 We also found that children born small for gestational age had higher caries prevalence than those born appropriate for gestational age. A similar relationship has been described by O’Connell and co-workers in an Irish population,21 but most previous studies have failed to find a link between being born small for gestational age and ECC.3,4,22 This also applies to low birthweight and caries 23,24 but it is important to note that low birthweight per se is not to the same as being born small for gestational age. We combined low weight and short length to define small for gestational age, which is common in endocrine studies but rare in previous caries studies. The fact that preterm or small for gestational age infants are more likely to develop caries has not been explained by our data, but it seems reasonable to assume that both biological factors such as defective enamel development and lifestyle-related determinants such as poor nutrition, sugar consumption, neglected oral hygiene, fluoride exposure and maternal health are involved. For example, a study in East London, UK, found a clear relationship between poor diet and preterm birth with low birthweight.25 It is also possible that a relationship between ECC and perinatal factors can be biased by a very high prevalence of caries, and the outcome may therefore differ with age, education level and poverty, as well as between high- and low-income countries.22,26

Neither smoking habit, lack of maternal education nor unemployment was found to influence the risk to develop caries. This is probably due to the homogenous population in this part of Sweden, with few smoking mothers, unemployed or with low education. Therefore, we acknowledge that the present findings may have limited external validity.

We found no significant correlation between ECC and the BMI of the child, which was as expected in the light of the complex U-shaped correlation that seems to exist; a recent meta-analysis of 14 studies has shown that caries frequency was significantly elevated in both underweight and overweight children.27 Therefore, further studies are required to investigate the confounding factors that might influence relationship between dental caries and BMI. The link between dental caries and metabolic risk factors has previously been investigated in adolescents, 28 but to the best of our knowledge, no studies in preschool children are yet available. In this context, our observation that the occurrence of caries correlated with elevated levels of fasting glucose was novel and interesting. Our findings concerning hyperglycaemia were consistent with reports in adults,29,30 but they need to be verified in larger a cohort of preschool children. Nevertheless, our data suggest that health professionals involved in the care of preterm infants, as

### TABLE 2 Prevalence of early childhood caries (ECC) at 5 y of age in preterm children and children small and large for gestational age.

| Variable            | n   | ECC (%) | RR  | 95% CI  | P-value |
|---------------------|-----|---------|-----|---------|---------|
| Full term (>36 wk)  | 195 | 14.9    |     |         |         |
| Preterm birth (32-36 wk) | 13  | 61.5    | 4.1  | 2.4-7.1 | <.001   |
| AGA                 | 174 | 14.5    |     |         |         |
| SGA                 | 24  | 33.3    | 2.3  | 1.2-4.5 | .036    |
| LGA                 | 10  | 40.0    | 2.8  | 1.2-6.4 | .054 (NS)* |

Note: Differences compared with full-term birth and appropriate gestational age, respectively, are expressed as relative risk (RR) with 95% confidence interval.

Abbreviations: AGA, appropriate for gestational age; LGA, large for gestational age, weight and/or length; SGA, small for gestational age, weight and/or length.

*NS, not significant. The P-value was calculated with Fisher’s exact test due to the small group size.
well as in the later well-being evaluations, should co-operate with dental professionals to support families in order to maintain oral health and reduce the risk of ECC.

As in all prospective clinical studies, several factors may have influenced the outcome. In this case, the size of the dental study group was relatively small due to the large dropout rate at the metabolic examination, which led to suboptimal power for some of the birth-related variables (especially large for gestational age at birth). The perinatal factors were balanced when compared with the full endocrine group, but there were significant differences concerning the mothers’ age, education, smoking habits and immigrant background. Nonetheless, these differences are unlikely to overestimate the obtained outcome, since ECC has a strong socioeconomic gradient and is significantly linked to maternal smoking.\(^1\)^\(^2\)^\(^9\) On the other hand, it is important to point out that the present study group was not representative for the average Swedish population, given that it included a larger proportion of children delivered by caesarean section. It is therefore possible, albeit unlikely, that this selection bias has influenced the relationship between ECC and being born small for gestational age.

An obvious strength of this project was that we collected all data in a systematic and quality-assured way from pregnancy over a period of 6.5 years. The relatively homogeneous population with children from stable socioeconomic conditions with a low prevalence of caries was also an advantage when examining the impact of perinatal factors. We also consider the fact that all the preterm children were moderately to late preterm as a strength, because earlier studies have included extremely, moderately and late preterm children. Another clear merit was that we included the early stages of caries, in contrast to previous studies in which the prevalence of caries was limited to cavitated lesions or filled teeth. This detection of early caries lesions is important as they reflect an ongoing disease activity rather than the disease history. Furthermore, the early detection of lesions allows secondary prevention and a non-operative, less invasive management of the disease.\(^2\)

### 5 CONCLUSION

Within the limitations of the present study, the results showed that preterm infants and children born small for gestational age display an increased risk of ECC. Children with caries had higher levels of fasting glucose but no other signs of the metabolic syndrome.

### ACKNOWLEDGEMENT

We thank Mr Anders Holmén at the Region Halland R&D Unit, Halland Hospital, for his skilled technical support.

### CONFLICT OF INTEREST

The authors declare no potential, perceived or real conflict of interest regarding the content of this manuscript.

### ETHICAL APPROVAL

The study was conducted according to the guidelines in the Declaration of Helsinki and approved by the Regional Ethical Review Board in Lund (approval number 44/2008, 2010/362, 2012/483). Written informed consent was obtained from all the participating parents at the start of the project, and verbal consent was obtained from the children who remained in the study at 6.5 years of age.

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**How to cite this article:** Boustedt K, Roswall J, Kjellberg E, Twetman S, Dahlgren J. A prospective study of perinatal and metabolic risk factors for early childhood caries. *Acta Paediatr*. 2020;109:2356–2361. [https://doi.org/10.1111/apa.15231](https://doi.org/10.1111/apa.15231)