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Jacobsson, Lennart; Jacobsson, Magnus E; Askling, Johan; Knowler, William C

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Perinatal characteristics and risk of rheumatoid arthritis

Lennart T H Jacobsson, Magnus E Jacobsson, Johan Askling, William C Knowler

Rheumatoid arthritis is a disease of unknown aetiology. Twin studies indicate the importance of genetic as well as environmental factors. In terms of environmental factors, few risk factors are well established, and, in practice, rheumatoid arthritis cannot be attributed to any specific exposure. Descriptive studies imply a birth cohort effect in the incidence of rheumatoid arthritis. We assessed perinatal characteristics in relation to the risk of adult rheumatoid arthritis and observed associations with several perinatal exposures, including high birth weight and low frequency of breast feeding.

Participants, methods, and results

We selected participants from a local register of all patients seen in the outpatient clinic at the Department of Rheumatology, Malmö University Hospital, southern Sweden, or by any of the three private rheumatologists in the same city. The register contains over 90% of all known cases of rheumatoid arthritis in the catchment area. We selected 77 subjects in this register (all patients who were born between 1940 and 1960 and were still living in Malmö) as cases (median age of onset of rheumatoid arthritis 46 years, 76% (59) positive for rheumatoid factor, 85% (65) with erosive disease). For each case we selected the consecutive four births of the same sex at the same delivery unit in Malmö as controls (n=308). Using the population and census registers, we identified 98 controls who were still living in Malmö at the time of the investigation for a restricted analysis including only controls (and the corresponding cases) who were still living in the department of rheumatology at Malmö University Hospital, or by any of the three private rheumatologists in the same city. The register contains over 90% of all known cases of rheumatoid arthritis in the catchment area. We selected 77 subjects in this register (all patients who were born between 1940 and 1960 and were still living in Malmö) as cases (median age of onset of rheumatoid arthritis 46 years, 76% (59) positive for rheumatoid factor, 85% (65) with erosive disease). For each case we selected the consecutive four births of the same sex at the same delivery unit in Malmö as controls (n=308). Using the population and census registers, we identified 98 controls who were still living in Malmö at the time of the investigation for a restricted analysis including only controls (and the corresponding cases) who were still living in the department of rheumatology at Malmö University Hospital, southern Sweden, or by any of the three private rheumatologists in the same city. The register contains over 90% of all known cases of rheumatoid arthritis in the catchment area. We selected 77 subjects in this register (all patients who were born between 1940 and 1960 and were still living in Malmö) as cases (median age of onset of rheumatoid arthritis 46 years, 76% (59) positive for rheumatoid factor, 85% (65) with erosive disease). For each case we selected the consecutive four births of the same sex at the same delivery unit in Malmö as controls (n=308). Using the population and census registers, we identified 98 controls who were still living in Malmö at the time of the investigation for a restricted analysis including only controls (and the corresponding cases) who were still living in the department of rheumatology at Malmö University Hospital, southern Sweden, or by any of the three private rheumatologists in the same city. The register contains over 90% of all known cases of rheumatoid arthritis in the catchment area. We selected 77 subjects in this register (all patients who were born between 1940 and 1960 and were still living in Malmö) as cases (median age of onset of rheumatoid arthritis 46 years, 76% (59) positive for rheumatoid factor, 85% (65) with erosive disease). For each case we selected the consecutive four births of the same sex at the same delivery unit in Malmö as controls (n=308). Using the population and census registers, we identified 98 controls who were still living in Malmö at the time of the investigation for a restricted analysis including only controls (and the corresponding cases) who were still living in the
cathetment area at the time of the investigation. One investigator (MEJ) undertook a structured review of the birth records of all cases and controls and extracted information on birth weight (categorised as < 3000 g, 3000-4000 g, and > 4000 g), length at birth, gestational length, weight of placenta, maternal diseases during pregnancy, maternal age, history of miscarriage, parity at time of birth of the case or control, length of hospital stay after delivery, start of breast feeding during the hospital stay after delivery, and paternal occupation (manual or non-manual worker). We calculated univariate and multivariate odds ratios by using conditional logistic regression to account for the matched design.

High birth weight (≥ 4000 g v 3000-3999 g) was positively associated with rheumatoid arthritis (odds ratio 3.3, 95% confidence interval 1.4 to 7.4: table), but low birth weight (< 3000 g v 3000-4000 g) was not. Initiation of breast feeding during inpatient care after delivery (0.2, 0.1 to 0.7), and paternal occupation (manual v non-manual worker; 2.8, 1.3 to 5.7) were also associated with rheumatoid arthritis. The associations between birth weight, initiation of breast feeding, and paternal occupation were not confounded by each other (table). We found no other significant associations. Analyses using the restricted sample of only controls living in the cathetment area at the time of the investigation resulted in similar risk estimates.

Comment

Our findings indicate that characteristics of the perinatal period may be of aetiological importance in the pathogenesis of rheumatoid arthritis. To our knowledge, this is the first study to assess markers of intrauterine and perinatal health in relation to adult rheumatoid arthritis, although preliminary data show that weight at 1 year of age is associated with rheumatoid arthritis, although preliminary data show.

Our findings may be explained by several factors, including the development of the immune system in utero, perinatal or postnatal modulation of the immune system, and unmeasured confounding factors. The strengths of this report include the population based design, the independent identification of controls, and the fact that information on exposure was recorded before the occurrence of the outcome.

Contributors: LTHJ participated in conception and design, analyses, and interpretation of the data, drafting, and final approval of the article. MEJ participated in conception and design, analyses and interpretation of the data, drafting, and final approval of the article. JA participated in conception and design, interpretation of the data, critical review, and final approval of the article. WCK participated in conception and design, interpretation of the data, critical review, and final approval of the article. LTHJ is the guarantor.

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Ethical approval: The study was approved by the ethics committee of Lund University.

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