Environmental Research 157 (2017) 198–205

Contents lists available at ScienceDirect

Environmental Research

journal homepage: www.elsevier.com/locate/envres

Effect of season of birth on cord blood IgE and IgE at birth: A systematic review and meta-analysis

Nugroho Harry Susanto[a,k,l], Don Vicendese[b], Agus Salim[c], Adrian J. Lowe[d], Shyamali C. Dharmage[d], Rachel Tham[d], Caroline Lodge[d], Frances Garden[e,m,n], Katie Allen[f], Cecilie Svanes[g], Joachim Heinrich[h,o], Michael J. Abramson[i], Bircan Erbas[j,*]

[a] School of Public Health, La Trobe University, Bundoora, Vic, Australia
[b] Cancer Council of Victoria, Melbourne, Vic 3004, Australia
[c] Department of Mathematics and Statistics, La Trobe University, Bundoora, Vic, Australia
[d] Allergy and Lung Health Unit, School of Population and Global Health, The University of Melbourne, Australia
[e] Woolcock Institute of Medical Research, The University of Sydney, Glebe, New South Wales, Australia
[f] Department of Allergy and Clinical Immunology and Department of Gastroenterology and Clinical Nutrition, Royal Children's Hospital, Melbourne 3052, Australia
[g] Centre for International Health, University of Bergen, Norway and Department Occupational Medicine, Haukelan, University Hospital, Bergen, Norway
[h] Institute of Epidemiology I, Helmholtz Zentrum München - German Research Center for Environmental Health, Ingolstädter Landstraße 1, 85764 Neuherberg, Germany
[i] School of Public Health and Preventive Medicine, Monash University, Melbourne
[j] School of Public Health, La Trobe University, Bundoora, Vic, Australia
[k] Indonesia Research Partnership on Infectious Diseases (INA-RESPOND), Jakarta, Indonesia
[l] Epidemiology and Biostatistics Division, Public Health Department, Faculty of Medicine, Padjadjaran University, Bandung, Indonesia
[m] South Western Sydney Clinical School, University of New South Wales, Liverpool, New South Wales, Australia
[n] Ingham Institute of Applied Medical Research, University of New South Wales, Liverpool, New South Wales, Australia
[o] Institute and Outpatient Clinic for Occupational, Social and Environmental Medicine, Inner City Clinic, University Hospital of Munich (LMU), Munich, Germany

ARTICLE INFO

Keywords:
Cord blood
IgE
Meta-analysis
Pollen
Season of birth

ABSTRACT

Background: Elevated cord blood IgE is important on the pathway to allergic disease. The association between season of birth and infant cord blood IgE is not well-established. Study findings differ on which birth season is associated with higher cord blood IgE risk and its magnitude. We conducted a systematic review and meta-analysis of studies on season of birth and cord blood IgE.

Methods: We searched Medline, Web of Science, Scopus and ProQuest Health databases, and reviewed reference lists of articles that met the inclusion criteria. All included studies measured IgE as a binary variable using various cut-off values. We performed multivariate-random-effects meta-analysis to handle an exposure with multiple categories of Season of Birth.

Results: Our search identified 275 records and 10 had sufficient data to be included in a meta-analysis. Relative to summer, winter birth had the greatest odds of high IgE (≥ 0.1 IU/ml), meta-analysis OR = 1.24 (95%CI: 1.01–1.52). A similar OR, was found for IgE ≥ 0.5 IU/ml, OR = 1.30 (95%CI: 0.99–1.71).

Conclusions: A winter season of birth was associated with statistically significant higher odds of elevated cord blood IgE at cut-off ≥ 0.1 IU/ml but borderline at cut-off ≥ 0.5 IU/ml. This winter effect is likely to be a marker for a range of other environmental exposures during specific stages of pregnancy, such as aeroallergen exposures, maternal infections and vitamin D levels. Further research is required to support our finding and to identify the exact mechanisms that lead to the winter season of birth effect on circulating IgE levels, as this may have implications for allergic disease prevention.

1. Introduction

Globally, allergic respiratory diseases continue to be a major public health burden in children. To date, we still do not have a full understanding of the causes of allergic respiratory diseases. However, we know that environmental factors, such as pollens, moulds, air pollutants and respiratory viruses, play a major part, along with genetic predisposition (Erbas et al., 2013). The adverse impact of outdoor exposures may begin at any time, with high risk windows for exposure including pregnancy, shortly after birth or within the first two years of

* Correspondence to: School of Public Health, La Trobe University, Room 129, Health Sciences 1, Bundoora, 3086 Victoria, Australia.
E-mail address: b.erbas@latrobe.edu.au (B. Erbas).

http://dx.doi.org/10.1016/j.envres.2017.05.026
Received 20 January 2017; Received in revised form 17 May 2017; Accepted 23 May 2017
Available online 30 May 2017
0013-9351/

life (Algert et al., 2012; Erbas et al., 2013).

In many studies of high risk children (at least one parent with history of allergic disease) and allergies in early life levels of Immunoglobulin E (IgE) measured in cord blood/at birth have shown to be a useful measure of subsequent risk of asthma and allergies (Ferguson et al., 2009; Kaan et al., 2000). A recent study by Bundhoo et al. showed that maternal IgE and cord blood IgE were highly correlated irrespective of the allergic status of the mothers suggesting that the maternal environment is important (Bundhoo et al., 2015).

Many factors influence IgE levels in cord blood with one of them being season of birth. Many studies have examined the association between season of birth and high cord blood IgE with mixed results. Studies have been conducted since the early 1990s in a range of locations with differences in geography, seasonal characteristics, and population characteristics from regions all over the world, but predominately in high income countries. Few used the same season of birth as the reference category when examining risk. For example, one study compared all seasons to summer (Scirica et al., 2007) and another compared all seasons to winter (Sadeghnejad et al., 2007). Furthermore, the studies that reported significant associations did not agree as to which season of birth had the greatest risk of high IgE, or how large was the actual risk.

The association between season of birth and allergic respiratory diseases has been studied extensively. It is hypothesized that season of birth is an important proxy for exposures at time of conception during pregnancy. For example, season of birth may act as a proxy for maternal exposures to UV-B as higher exposures during pregnancy may lower risk of subsequent allergic disease (Camargo et al., 2011). It may also be a proxy for the seasonal variation of maternal nutrient intake (Watson and McDonald, 2007). Mother's response to viral or bacterial infections in autumn and winter might lead to increased immune response in infants born in spring and summer (Sullivan Dillie et al., 2008).

It is important to synthesise these findings to clarify which months pose the greatest risk, whilst acknowledging differences in latitude, climatic conditions and populations. In doing so, we may be better placed to understand the environmental conditions that contribute to cord blood IgE levels. For example, if cord blood IgE is particularly high in infants born in spring compared to other seasons, then this may point to specific environmental allergens at birth or a particular stage during pregnancy which have adverse effects on subsequent immune development. In this review, we attempt to qualitatively synthesise all of the studies that have examined the association between the season of birth and high IgE in cord blood or at birth, and where possible, quantify the magnitude of these associations by using meta-analytic techniques.

2. Methods

In this systematic review and meta-analysis, we followed the MOOSE guidelines for identifying observational studies for systematic review and meta-analyses (Stroup et al., 2000).

2.1. Inclusion criteria

In order for a study to be included in this review, it had to focus on humans, be published in English, and measure the association between the outcome of IgE in cord blood, or in the first week of life, and the season of birth as the exposure. We considered the first week because evidence suggests a significant correlation between IgE in both cord blood and blood in the first 5 days of life (Hansen et al., 1992). Only studies that provided effect sizes, or sufficient data to allow effect sizes to be calculated, were included in the meta-analysis.

2.2. Search strategy

A literature search was conducted using bibliographic databases: Medline (PubMed), Web of Science, Scopus, Google Scholar and ProQuest Health. The search terms are listed in the online Sup. Table 1. An additional manual search was also conducted based on citations of all articles that met the inclusion criteria. The abstracts of all identified articles were reviewed by authors BE, NHS and AS for initial inclusion; then full papers were reviewed by NHS and BE based on the inclusion criteria.

2.3. Assessment of quality and risk of bias

Two authors (NHS and RT) independently assessed the quality of each study using a validated quality assessment framework (Zaza et al., 2000) in combination with the Cochrane Collaboration risk of bias assessment (Sterne and Reeves, 2014). Quality was assessed using a checklist: description of the study population and how they were selected; how exposure (season of birth) was measured and whether this was valid and/or reliable; whether the outcome (cord blood IgE or a week after birth IgE) measures were valid and/or reliable; the appropriateness of the statistical testing; the appropriateness of controlling potential confounders (maternal age, gestational age, birth order, maternal ethnicity, maternal allergic disease during pregnancy, parental atopy); appropriateness of controlling for potential bias (i.e. selection bias, recall bias, measurement bias, analytic biases related to sample sizes and statistical methods); and whether problems with data analysis limited the interpretation of the results. Any differences between reviewers were resolved by discussion and consensus that led to agreement on final scores. Any paper that reported results as descriptive statistics and correlations which matched their aims were also assessed.

2.4. Data extraction

We extracted the following data from each study: study design; country and whether the city was urban or rural; sample size, IgE measurement method, the grouping of IgE levels and the cut-off that was used for the categorisation if any were reported in the paper, month and/or season of birth; effect estimates including 95% confidence intervals (CI); potential variables considered as confounders and/or effect modifiers.

2.5. Statistical analysis

Three authors (BE, NHS and DV) assessed whether papers could be included in the meta-analysis. Since the exposure of interest (seasons of birth) has four categories, which means that from each study we need to extract three odds-ratios that compare three seasons against the reference season (e.g. Summer). Generally speaking, odds-ratios from the same study are correlated and this within-study correlation cannot be handled by standard meta-analysis. We therefore decided to conduct multivariate random-effects meta-analysis that were developed to handle meta-analysis with multiple outcomes and/or exposure with multiple categories (White, 2011).

One key requirement of multivariate random-effects meta-analysis was determining the amount of correlation among odds-ratios from the same study. To compute the correlations, we needed the raw counts of subjects for each season of births and outcome category (low/high IgE). Hence, only studies that reported these raw counts could be included in our meta-analysis. Studies without this information were excluded and these include studies that reported adjusted or unadjusted odds ratios without providing subject counts by season of birth and outcome. For studies that reported the counts by month of birth, we aggregated the count by season of birth according to the study location. Studies used different cut-offs to define high IgE levels and to investigate the impact of using different cut-offs on our meta-analysis estimate, we performed two separate meta-analyses involving: (a) studies that used IgE $\geq$ 0.1 IU/ml and (b) studies that used IgE $\geq$ 0.5 IU/ml. We chose these two cut-offs as these were the cut-offs used by the majority of studies