

# **The impact of COVID-19 lockdown on infants' coronavirus exposure and routine healthcare access in Ireland: the CORAL study at 6 months.**

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## **Introduction**

The public health strategy during the SARS-CoV-2 (COVID19) pandemic of 2020-2021 led to profound changes in social behaviour, affecting not only familial but also wider social interactions in settings such as workplaces, schools and day care facilities. These changes may have altered viral and bacterial interchange.

A significantly decreased diversity of gut and skin microbiota has been demonstrated in allergic individuals compared to non-allergic subjects<sup>1</sup>. The **CORAL** study is a longitudinal study of the impact of the Coronavirus Pandemic on Allergic and autoimmune dysregulation of infants born from March - May 2020, during Ireland's first lockdown (Ireland formally entered national lockdown on March 27<sup>th</sup> 2020, though severe restrictions had been gradually escalated for the 2 weeks prior to that date. The first release of lockdown was on June 8<sup>th</sup> 2020). CORAL will follow children initially until they are 2 years old, with stool sampling at 6, 12 and 24 months for microbiome diversity analysis and allergy testing and blood RNA and epigenomic testing at 12 and 24 months

Now, in the immunisation phase of the pandemic response, attention is shifting from immediate population protection during waves of COVID-19 to the health care and social consequences of both the pandemic and the societal disruption created by lockdown. There

are particular concerns that important medical care (such as infant immunisations) may have been delayed, or even refused, due to patient or family concerns about infection risk when attending health care facilities also managing COVID-19.

We report here the impact of COVID-19 lockdown on health care access, completion of immunisation and COVID-19 infection rates in Irish babies to 6 months of age enrolled in the CORAL STUDY.

## **Methods**

Ethical approval was obtained from the National Research Ethics Committee (20-NREC-COV-067) and the participating hospitals' ethics committees. Informed written parental consent was obtained.

Invitations were sent to families of term, singleton babies born in 2 major maternity hospitals in Dublin, during March to May 2020. Exclusion criteria were pre-birth PCR-proven SARS-CoV-2 infection in a parent or co-dwelling person, intravenous antibiotics in the neonatal period, multiple birth or major congenital anomaly.

At 6 months (September - November 2020), families were sent a questionnaire and a stool sample collected for microbiome analysis (results will be reported elsewhere). Families were also offered point-of-care SARS-CoV-2 antibody testing (VivaDiagTMSARS-CoV-2 IgM/IgG Rapid Test) for the infants, however escalation of national travel restrictions in response to the second surge of COVID-19 in September and October 2020 restricted access to this testing for some infants.

## **Results**

365 infants were enrolled. 195 babies (53.4%) were male, 94.5% were of "White Irish" or "Any Other White" background and 94% of mothers were educated to third level or higher. The average birth weight was 3.5kg. Most babies were either first-born (45%) or second-born (37%). In infants with siblings (n=201), atopic dermatitis was most common allergic condition reported (15.4%), followed by asthma (12.4%) and food allergy (11.4%). Allergic

rhinitis was the most commonly reported atopic condition in both mothers (36%) and fathers (30%).

360 six-month questionnaires were completed. Exclusive breastfeeding rate at 6 months was 38%, a further 15% were receiving breastmilk and infant formula. 92% were having regular solids with a median weaning age of 5 months (range 3-6 months). The rates of introduction of allergenic foods such as egg and peanut are outlined in Table 1.

99% of infants had been fully vaccinated according to the Irish Primary Childhood Immunisation Schedule and 7.5% of babies had been admitted to hospital in the first 6 months. Antibiotics had been prescribed for 25 infants (7%) and 5 of those infants had received more than one course. Possible allergic reactions to a food or environmental substance were reported by 47 children (13%), but on elaboration most described a flare of eczema without identifying a particular allergen.

By the age of 6 months, 30 (8.3%) had had community testing for SARS-CoV-2 PCR due to symptoms or known close contact, and 2 (0.5%) were PCR positive. 268 (73%) of babies had point-of-care lateral flow immunoassay testing at 6 months as part of the study, of whom 3(1.1%) returned positive results for IgM and IgG SARS-CoV-2 antibodies. One infant (as above) had known prior PCR-proven SARS-CoV-2 infection but there two further cases with no known COVID-19 exposure. Of these 1 was PCR positive (indicating very recent or current infection) and the other was PCR negative. Overall 4 babies (1%) were shown to have immunological evidence of exposure to SARS-CoV-2 infection before the age of 6 months.

## Discussion

It is reassuring that this population of infants born during lockdown had been presented as advised for routine healthcare such as immunisations, actually at even higher rates than national norms. Weaning rates were in line with national trends in Ireland, and despite the low rates of egg and peanut introduction, these are in line with national data, so weaning to allergenic foods did not seem to have been impacted by heightened fear of adverse outcomes or risk of needing to emergency care during the pandemic. In contrast the overall rate of attendance at hospital for any reason (7.5%) or any use of antibiotics were lower

than expected, supporting our previous data about significant changes in circulation of virus related illnesses in the early stages of the 2020 lockdown<sup>2</sup>.

This self-selected cohort of infants is largely representative of the overall Irish population.<sup>3 4</sup> The proportion of first-borns (45%) is higher than the national average (38.8%) but these larger maternity hospitals (more than 8000 deliveries each per annum) have high rates of primigravida patients.<sup>4</sup> A notable difference is the level of maternal education. In the 2016 Irish census 43.2% of women were educated to third level compared with 94% of mothers in this study.<sup>5</sup> This, along with mothers working from home during lockdown, is likely contributing to the atypically high percentage of Irish infants still breastfed at 6 months; in Ireland this figure is approximately 15%<sup>6</sup>. The rate of reported food allergy in siblings of this cohort (sourced from unconfirmed parental reports rather than from health care record searches) is higher than the general population, which may have contributed to parental desire to enrol in this study.<sup>7</sup>

The rare (1%) positive SARS-CoV-2 antibody tests at 6 months suggesting recent or current infection imply that in Ireland, at least, newborn babies, traditionally considered to be particularly vulnerable to viral infection, appear to have been largely protected from SARS-CoV-2 exposure during the first COVID-19 lockdown in 2020.

The next stage of the CORAL study commenced in February 2021. It involves a review of the participants at 12 months with skin prick testing for common food and aeroallergens, a further questionnaire, stool sample and SARS-CoV-2 antibody test and peripheral blood sample for RNA sequencing to determine host immune responses to the COVID-19 lockdown.

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## Conflict of interest

JO'BH is a Board member of Clemens Von Pirquet Foundation. No other conflicts declared.

## Table. Introduction of allergenic foods at 6 months

Allergenic Foods at 6 months	Introduced Food (%) Total N=360
Egg	95 (26%)
Peanut	49 (13.6%)
Treenut	12 (3.3%)
Wheat	151 (42%)
Fish	59 (16.4%)
Dairy	166 (46%)
Dairy Alternatives	17 (4.7%)