

Supplementary File (SF1)

Postulated cumulative socio-environmental alterations and maternal behavioural modifications during COVID-19 lockdown that could have influenced the births of VLBW and ELBW infants: a descriptive review of existing evidence from published literature.

1. Pregnancy associated stress, anxiety and support systems

Psychological stresses increase the likelihood of VLBW and ELBW births. Positive benefits from familial support have been reported.¹ Male partner involvement on reducing premature births rates has been suggested.² Compared to women who reported no partner involvement and support during pregnancy, those who had it reported better psychological well-being.³ There is strong evidence that pregnancy-specific anxiety, depression and stress increase the likelihood premature deliveries.⁴ Impacts of on-call work during pregnancy in relation to stress and sleep are not well established.⁵ Measures of psychological distress including alterations in blood corticotrophin-releasing hormone (CRH) levels and cortisol are associated with VLBW births.⁶ The biologic pathways underlying stress-induced VLBW births remain poorly understood.⁷ On the other hand, women could be stressed by confinement, overwork, distance from family and friends, fear of becoming infected COVID-19 as well as the fear of attending health services.

2. Work related stress, physical work, shift work and on-calls

Studies suggest an association of shift work, fixed night shifts and long working hours during pregnancy with VLBW and ELBW deliveries.^{8,9} Women working more

than 55.5 hours (vs 40 hours) per week had a 10% increase in the odds of having a preterm births.⁸ Danish National birth cohort study associated shift work with an increase in small-for-gestational-age (SGA).¹⁰

Physically demanding work while pregnant increases premature births as per systematic review and meta-analysis.^{8,11} A threefold increase in preterm births was reported in women whose daily work entailed trunk bending for over one hour.¹² Bed rest in hospital or at home is widely recommended as a conventional practice to prevent premature deliveries through the possible reduction of uterine activity. While sufficient rest and relaxation seems appropriate, Cochrane review concluded neither supporting nor refuting the use of prolonged bed rest at home or in hospital, to prevent premature births.¹³

3. Environmental factors, temporal variations, air pollution

A study from USA exploring temporal patterns of prematurity observed a periodicity for premature birth rates.¹⁴ Association between ambient air pollution (AAP) exposure during pregnancy and prematurity has been reported.^{15,16,17} Particulate matter, nitrogen dioxide, ozone, and carbon monoxide were the most commonly used markers of AAP.^{16,17} Sulphur dioxide (SO₂) was the largest contributor to increase PTB and other agents were particulate matter (PM)_{2.5} micron, PM₁₀ micron and NO₂.¹⁵ One study from Wuhan, China linked premature births to the atmospheric pollutant, vanadium.¹⁸ The relationship between atmospheric temperature and seasonal fluctuations to preterm births has been suggested⁰¹⁹ European pattern is discerned with a spring peak and in Asia and US a seasonal variance of up to 5-10% has been reported.¹⁹

Cumulative contribution to AAP improvement during the COVID-19 lockdown by the reduction in all modes of transport, reduced consumption of diesel and petrol, reduced production and distribution of goods and closure of factories, all led to reduced environmental pollution in UK and Europe during the lockdown.²⁰

4. Socioeconomic factors and financial strain

'*Growing up in Ireland survey*' calculated the index for LBW arising from PTB and intrauterine growth restriction (IUGR) and an association with parental education and environmental conditions was observed.²¹ The UK Bradford study found that a new variable of interest, financial strain, was associated with a significant increase in prematurity.²² Financial assistance offered by the Irish Government during lockdown to businesses, self-employed and employees who were temporarily laid off, possibly could have reduced financial strain to a certain extent on the pregnant families in the midst of the population wide anguish due to COVID-19 induced economic hardship.

5. Maternal nutrition, opportunities for wellbeing and exercise

Observational data suggest the influence of maternal under nutrition in spontaneous premature birth, which support a role for optimal maternal pre-pregnancy and in-pregnancy nutritional status in determining gestational length.²³ A low maternal body-mass index (BMI) was associated with spontaneous preterm births²⁴ Compared to no exercise during pregnancy, those taking appropriate leisurely exercise lowered the risk of preterm birth and placental weight gain could partially mediate the association between exercise during pregnancy and prematurity.^{25,26}

6. Reduction of chances for infections during pregnancy

Susceptibility to infectious diseases is often modified during pregnancy. Alterations in immunity to allow for the foetal allograft to implant and thrive combined with the anatomical and physiological modifications underlie these susceptibilities.²⁷ It has been shown that relationship satisfaction reduces infectious diseases in pregnancy.²⁸ Behavioural changes promoted during and prior to the lockdown, including social distancing, enhanced hand hygiene and use of face masks potentially reduced the chances of common viral infections during pregnancy. In addition, the closure of crèche, day-care centres, child minding facilities and play schools that normally 'bring home' common infections further reduced the potential for infective agent exposure.²⁹ Adoption of WFH policies by pregnant women and their partners may have further reduced exposure to the 'microbial world' of the adult population. Consequently, there may have been a reduction in the likelihood of Influenza, parvovirus B19 and congenital cytomegalovirus (CMV) that are more significant infections during pregnancy, with acknowledged associations with VLBW and ELBW.^{29,30,31,32}

7. **Daily commuting and road traffic incidents**

Irish national lockdown has brought down overall vehicular traffic, reduced the commuting to and from work locations, avoided early start and late return to home, attenuated traffic-related stresses and improved atmospheric air pollution. Arguably, the potential for crashes involving pregnant women should be low as well. After a single crash, pregnant drivers had increased rates of PPRM and PTB.^{33,34} Evaluation of potential adverse foetal outcome using a 26 weeks pregnant woman manikin has previously demonstrated significant harm using common accident scenarios.³⁵ An observational study reported increased prematurity following air

travel, however large multi-centric studies would be warranted before drawing conclusions and the contribution to our study cohort would be low based on population characteristics.³⁶

8. Domestic abuse or intimate partner violence

During a lockdown or similar measures, depending on the socioeconomic factors and population characteristics, there is potential for upward or downward trends in domestic abuse or Intimate partner violence (IPV).³⁷ IPV is an important public health problem and an association between IPV and preterm birth has already been demonstrated. Prevalence of IPV was 14.9% in an Australian study and the main precipitating cause of PTB was antepartum haemorrhage.³⁸ Psychological abuse by partner was associated with increased risk prematurity in one South Indian study.³⁹

9. Cigarette smoke, coffee, alcohol, prescription drugs and street drugs

Approximately 11% of Irish women smoke during pregnancy and 28% of those who smoke while pregnant had SGA infants compared to non-smokers at 13%.³⁹ Both active and passive (second-hand or environmental) tobacco smoking during pregnancy is associated with risk of SGA and prematurity.^{41,42} PTB has been reported for women with drug dependence, cocaine and poly-substance being at the highest risk.⁴³ Studies evaluating alcohol consumption during pregnancy are often overshadowed by bias attributable to unmeasured confounders and varying or no impact on prematurity rates has been reported.⁴⁴ Meta-analysis showed that high consumption of coffee during pregnancy is associated with low birth weight (LBW).⁴⁵ On the other hand certain herbal preparations claim myorelaxant, anti-inflammatory and immunomodulatory properties and were reported as useful in preventing prematurity associated with inflammation and infection.⁴⁶

10. Optimising maternal immunizations

Maternal immunization schedules are increasingly coming under the spotlight as part of the 'life-course' immunization programmes for the role that they play in improving maternal, foetal, and neonatal health.⁴⁷ Even though not primarily targeted to reduce VLBW or ELBW deliveries, influenza vaccination during pregnancy indirectly reduces prematurity through the reduction of maternal morbidity.⁴⁷

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