

Executive summary

Every child has the right to be wanted, well-born and registered as an individual at birth

Objectives

- The objectives of this review were to critically appraise the available evidence from published systematic reviews, meta-analyses, narrative reviews and in the absence of reviews original studies to:
 - Identify the determinants of preterm/small for gestational age (SGA)/low birth weight (LBW)/intrauterine growth restricted (IUGR) births and
 - Ascertain the effectiveness/efficacy of interventions to prevent preterm/SGA/LBW/IUGR births
- This review will help to guide Toronto Public Health initiatives to address the issue of preterm/SGA/LBW/IUGR births

Background

- Preterm and LBW (including IUGR) births constitute a major health problem worldwide including Canada.
- In the year 1997 LBW rates among all live births in Canada, Ontario and Toronto were 5.8, 5.9 and 6.6% respectively. However, results of a study by the Central East Health Information Partnership estimate that in 1997, 2.3% of births to Ontario residents and 3.2% of births to Toronto residents were not included in the official Ontario vital statistics data.
- In 1997 the preterm birth rate for Canada (excluding Ontario) was 7.1%.

Data accuracy

- Accurate data collection and analyses are a prerequisite for the evaluation of the effectiveness of any intervention aimed at the population at risk.
- Concerns about data accuracy have prevented the Canadian Perinatal Surveillance System of Health Canada from including the data from the Province of Ontario in its many peer-reviewed publications.
- Preterm birth rates for Ontario and Canada (including all provinces and territories) are not included in this report due to concerns about accuracy in the reporting of gestational age in the Ontario vital statistics data.
- Results of a study by the Central East Health Information Partnership show that the percentage of unregistered births (birth events not included in the official Ontario vital statistics data) in Ontario increased from less than 1% in the early 1990s to over 3% in 1998. The percentage of unregistered births is higher among births to mothers under 20 years of age and in LBW and preterm births. The rates of preterm/SGA/LBW/IUGR

births are likely to be underestimated in the Province of Ontario and Toronto. The introduction of birth registration fees by some municipalities (including Toronto) in 1996/1997 appears to have negatively affected the registration process. In the event of an early neonatal death there is no incentive for parents to register the birth of their child. This could account for a serious element of bias in the reporting of vital statistics in Ontario.

Methodology

- A comprehensive search strategy was carried out. Twelve electronic databases, relevant book chapters, recently published issues of five key journals and reference lists of the identified articles were searched. Explicit inclusion and exclusion criteria were developed. Selected primary data were included when review(s) were not available or studies were reported after the review. Methodological quality of included reviews and primary studies was assessed. Data were abstracted from included reviews and primary studies.
- The strength of the evidence for each determinant was assessed. Determinants with proven association (information from the epidemiological studies satisfying most of the causality criteria), possible association (information from the epidemiological studies satisfying some of the causality criteria but further research is needed), and no association (information from the epidemiological studies not indicative of causal association) were identified. Potential determinants for which no information was available were also identified.
- The strength of the evidence was assessed for various interventions/strategies to prevent preterm/LBW/SGA/IUGR births. Interventions/strategies were identified as having strong evidence of effectiveness (cumulative evidence from well designed meta-analyses or systematic reviews indicative of effectiveness), probable evidence of effectiveness (some evidence from systematic reviews or randomized controlled studies or clinical studies indicative of effectiveness), evidence that they may be effective (evidence from clinical and/or epidemiological studies of the causality for the determinant, however intervention studies are non-existent or poorly designed) or evidence that they were not effective (cumulative evidence from well designed meta-analyses or systematic reviews indicative of ineffectiveness). Interventions/strategies were identified for which there was a lack of or inadequate information.

Determinants of preterm/LBW/SGA/IUGR births

The determinants were evaluated individually for the purpose of simplicity and to identify the impact of each factor in this report. However, the problem of preterm/LBW/IUGR/SGA births is multifactorial. An evaluation of interaction of various factors in the causation of adverse pregnancy outcomes was not always possible.

A. Determinants with proven association:

- a. A short (<18 months) and a long (>60 months) birth interval
- b. Previous history of preterm/LBW births
- c. Race/ethnicity
- d. Extremes of maternal age
- e. Maternal malnutrition
- f. Bacterial vaginosis
- g. Urinary tract infection
- h. HIV infection
- i. Chronic stress
- j. Low socioeconomic status
- k. Tobacco use
- l. Heavy alcohol use
- m. Cocaine use
- n. Passive smoking/environmental tobacco smoke exposure
- o. Violence/abuse
- p. Antenatal care
- q. Placental factors
- r. Multiple births

B. Determinants with possible association but further research is needed:

- a. Maternal parity (first born)
- b. Marital status (single)
- c. Inadequate weight gain during pregnancy
- d. Short maternal height
- e. Low prepregnancy weight
- f. Maternal medical/pregnancy associated conditions
- g. Maternal trichomoniasis infection
- h. Periodontal infection
- i. Heavy caffeine use
- j. Marijuana use
- k. Licorice ingestion
- l. Environmental pollution
- m. Noise
- n. Occupational hazards
- o. Physically demanding work and prolonged standing at work
- p. Uterine factors
- q. Pharmacological factors
- r. Paternal factors
- s. Genetic factors

C. Determinants with no association:

- a. Fetal sex
- b. Maternal use of electromagnetic beds

D. Determinants for which no information is available:

- a. Alternative medicine
- b. Herbal medicines

Interventions/strategies to prevent preterm/LBW/SGA/IUGR births

A. Interventions/strategies with strong evidence of effectiveness

- a. Primary prevention
 - i. Smoking cessation and relapse prevention as a routine component of prenatal care, particularly interventions that include intensive counseling, multiple contacts, provision of supportive material and follow up.
 - ii. Treatment of infection
 - iii. Screening mothers with previous history of preterm/LBW births for infection
 - iv. Promotion of balanced nutritious diet for all pregnant women. The nutritional status of all pregnant women should be assessed. Provision of nutritious food to mothers identified as having limited resources to meet the demands of pregnancy may be beneficial.
- b. Tertiary Prevention
 - i. Administration of glucocorticoids to mothers with threatened preterm labor to reduce subsequent complications in the newborn infants

B. Interventions/strategies with probable evidence of effectiveness

- a. Primary prevention
 - i. Promotion of adequate weight gain during pregnancy*
 - ii. Promotion of optimal nutrition during the preconceptional period*
 - iii. Provision of antenatal care which provides an opportunity for individual assessment as well as diagnosis and appropriate management of maternal medical conditions
 - iv. Early enrollment of pregnant adolescents in prenatal programs
 - v. Home visiting and psychosocial support to pregnant adolescents
 - vi. Supplementation of calcium for women at risk of developing pregnancy induced hypertension or with low dietary intake of calcium*
 - vii. Provision of psychosocial support to high risk women experiencing chronic stress*
- b. Tertiary Prevention
 - i. Transport of high risk women to perinatal centers for delivery and further management

* Research regarding the effectiveness of specific strategies is required

C. Interventions/strategies which may be effective

- a. Primary prevention
 - i. Reduction of exposure to noise*
 - ii. Reduction of work related stress, physical exertion and prolonged standing*
 - iii. Identification and responding to abuse/violence*
 - iv. Supplementation of zinc and magnesium
 - v. Prevention of cocaine use*
 - vi. Identification of women using excessive alcohol during pregnancy and strategies to avoid heavy alcohol use*
 - vii. Reduction of exposure to environmental toxins*
 - viii. Legislation regarding regulation of artificial reproductive technologies*

- ix. Fish oil supplementation particularly to women with previous preterm births

* Research regarding the effectiveness of specific strategies is required

D. Interventions/strategies which are not effective

- a. Primary prevention
 - i. Supplementation of high protein diet during pregnancy
 - ii. Salt restriction
 - iii. Psychosocial support for all women
- b. Secondary prevention
 - i. Prenatal education regarding signs and symptoms of preterm labor
 - ii. Home uterine activity monitoring
 - iii. Tocolytics
 - iv. Bedrest
 - v. Hydration

E. Interventions/strategies for which there is lack/inadequate information

- a. Primary prevention
 - i. Supplementation of multivitamins, Vitamins A, B, C, D, E
 - ii. Supplementation of minerals
 - iii. Interventions regarding interaction of micronutrients
 - iv. Nutritional advice
 - v. Interventions regarding interaction between nutritional, social and psychological factors
 - vi. Interventions to modify stressors
 - vii. Treatment of certain maternal infections
 - viii. Efficacy of nicotine replacement therapy for heavy smokers
 - b. Secondary prevention
 - i. Screening methods to identify high risk women
 - ii. Methods of early prediction/diagnosis of preterm labor (clinical scoring system or monitoring cervical changes)
 - iii. Cervical cerclage
 - iv. Sedation
- Supplementation of folic acid (conclusive evidence of reduction of neural tube defects) and iron (improvement in maternal hematological parameters) have shown benefit with regards to maternal/fetal health. Though these interventions have not reduced preterm/LBW births, they should be promoted.

Conclusions

- Preterm/LBW/SGA/IUGR births constitute an enormous medical, societal and financial problem.
- A concerted effort for estimating the true incidence of the issue in Toronto, identifying modifiable factors within the population of Toronto and methods for implementing interventions are needed.
- There are multiple determinants of preterm/LBW/SGA/IUGR births. It is likely that there is interaction between these determinants. Therefore, the intervention programs should target multiple determinants. Practice based on

the strength of evidence is of utmost importance to reduce the incidence and subsequent complications.

- There are certain interventions/strategies for which effectiveness has not been proven, but causal associations are of sufficient strength to recommend intervention based on the precautionary principle (eg, promoting awareness of adverse effects of harmful substances such as cocaine, exposure to prolonged work related exertion).
- Women with a previous history of preterm/LBW births are at increased risk for a subsequent preterm/LBW birth. Adequate support from the preconceptional period including monitoring for identified causes of previous adverse outcomes, adequate nutrition, pregnancy spacing, avoidance of harmful substances/strenuous working conditions/chronic stress, screening and treatment of infection, and socioeconomic support may help to reduce the risk of subsequent preterm/LBW birth.
- Although beyond the scope of this paper, strategies/interventions directed towards the entire population to prevent smoking/exposure to environmental tobacco smoke, alcohol use, infection, violence/abuse, undernutrition, exposure to environmental toxins, and occupational hazards may help to reduce the risk of preterm/LBW births as well as other untoward health outcomes.
- Research regarding pathways to preterm/LBW/SGA/IUGR births is ongoing. There is a need to understand the mechanisms underlying the differential effects of socioeconomic disparities within society on preterm/LBW. Stress/psychosocial/socioeconomic factors are important determinants. The understanding of the effects of stress is evolving. Stress could be a final pathway for many other determinants such as unhealthy lifestyles, abuse/violence, work related stress, prolonged physically demanding work, low levels of social support, and poor nutritional status. A combined effect due to physical demands, exposure to environmental toxins, and stress is suspected.
- Further research is needed to understand the biological mechanisms and modifiable factors associated with racial/ethnic differences in rates of preterm/LBW.
- Research regarding contributing factors and effective interventions to reduce the risk of preterm/LBW births to women in their late fertile age is also needed.
- Secondary prevention measures for predicting preterm labor although promising, requires further research. Bedrest and maternal hydration have not been effective in treating threatened preterm labour. Educational programs to increase awareness of the signs and symptoms of preterm labour have been ineffective in reducing the incidence of preterm births. Tocolytic therapy is effective in reducing the rate of delivery within 48 hours. This allows for the administration of corticosteroids to the mother in an attempt to improve fetal lung maturity, but has not reduced the risk of preterm/LBW births or improved neonatal outcomes and has been associated with serious maternal complications. Further research is needed to identify safe interventions that

prevent preterm birth or arrest preterm labour in its early stages. It is still important to implement and evaluate strategies that help all women recognize the signs of early preterm labour and respond by seeking early medical attention.

- Tertiary prevention measures such as maternal transfer to a tertiary care center for further management and administration of glucocorticoids have shown benefit in the overall outcome of preterm/LBW infants.