



**Risks of Low Birth Weight, Small-for-Gestational Age and
Preterm Births Following the Economic Collapse in Iceland 2008**

Védís Helga Eiríksdóttir

**Thesis for the degree of Master of Public Health Sciences
Centre of Public Health
School of Health Sciences
University of Iceland**



HÁSKÓLI ÍSLANDS

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**Tíðni lágrar fæðingarþyngdar, léttbura- og fyrirburafæðinga í kjölfar
efnahagshrunsins á Íslandi árið 2008**

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Abstract

Infants born small or preterm have increased rates of mortality and morbidity throughout childhood and into adulthood. Stressful events have been suggested as potential contributors to preterm birth (PB) and low birth weight (LBW). We aimed to study the effect of the 2008 national economic collapse in Iceland on the risk of these adverse birth outcomes.

The study population constituted all Icelandic women giving birth to live-born singletons from January 1st 2006 to December 31st 2009. LBW infants were defined as those weighing <2500g at birth, PB infants defined as those born before 37 weeks of gestation and small-for-gestational age (SGA) defined as infants with birth weight less than two standard deviation below the mean on a fetal growth curve. Exposure to the collapse of the Icelandic banking system was modeled with calendar time. We used logistic regression to estimate odds ratios [OR] and the corresponding 95 percent confidence intervals [95%CI] of these adverse birth outcomes by exposure to calendar time of the economic crisis, i.e. after October 6th 2008.

Compared to the preceding period, we observed a short-term increase in LBW deliveries following the economic collapse (aOR=1.24, 95% CI [1.02, 1.52]), particularly among children born to women younger than 25 years (aOR=1.85, 95% CI [1.25, 2.72]) and mothers not working (aOR=1.59, 95% CI [1.10, 2.31]). Similarly, we found a tendency towards higher incidence of SGA births (aOR=1.14, 95% CI [0.86, 1.51]), particularly among children born to women younger than 25 years (aOR=1.85, 95% CI [1.08, 3.19]) and to women not working (aOR=1.84, 95% CI [1.09, 3.10]). We found no change in the risk of PB. The results suggest a short term increase in incidence of low birth weight following the dramatic collapse of the Icelandic national economy. The increase in LBW seemed driven by reduced fetal growth rate rather than shorter gestation.

Ágrip

Börn sem fædd eru of létt eða fyrir tímann eru í aukinni áhættu varðandi nýburadauða auk þess sem þau eiga oft við heilsufarsvandamál að stríða þegar fram líða stundir. Þættir sem hafa verið nefndir sem mögulegir orsakavaldar léttbura- og fyrirburafæðinga eru meðal annars streituvaldandi atburðir og sálræn streita. Markmið þessarar rannsóknar var að skoða áhrif efnahagshrunsins á Íslandi árið 2008 á tíðni léttbura- og fyrirburafæðinga.

Rannsóknin náði til allra íslenskra kvenna sem höfðu eignast lifandi fædda einbura á tímabilinu 1. janúar 2006 til 31. desember 2009. Léttburar voru skilgreindir sem börn sem vógu <2500 grömm við fæðingu, fyrirburar sem þau sem fæddust fyrir 37. viku meðgöngu og vaxtarskert börn sem voru undir tveimur staðalfrávikum undir meðalþyngd á fósturvaxtarkúrfu. Útsetning var hrún íslenska bankakerfisins, skilgreint með tíma. Börn sem fæddust eftir hrún eru álitin vera útsett fyrir efnahagshruninu og þau sem fæddust fyrir hrún talin ekki útsett. Lógistísk aðhvarfsgreining var notuð til að meta gagnlíkindahlutfall [OR] og samsvarandi 95 prósent öryggisbil [95% CI] þessara óhagstæðu fæðingaútkomna eftir útsetningu.

Það var marktæk skammtíma aukning á léttburafæðingum á tímabilinu eftir hrún, miðað við undanfarandi tímabil (aOR=1.24, 95% CI [1.02, 1.52]), sérstaklega á meðal yngri mæðra (<25 ára)(aOR=1.85, 95% CI [1.25, 2.72]) sem og kvenna sem voru ekki í vinnu (aOR=1.59, 95% CI [1.10, 2.31]). Ennfremur, virðist vera ákveðin tilhneiging í átt að aukinni tíðni vaxtarskertra barna (aOR=1.14, 95% CI [0.86, 1.51]), sérstaklega á meðal yngri mæðra (<25) (aOR=1.85, 95% CI [1.08, 3.19]) sem og mæðra sem ekki voru í vinnu (aOR=1.84, 95% CI [1.09, 3.10]). Engin breyting var á tíðni fyrirburafæðinga á tímabilinu. Niðurstöðurnar benda til skammtíma aukningar á tíðni léttburafæðinga í kjölfar hruns íslenska efnahagskerfisins. Þessi aukning virðist vera tilkomin vegna minni vaxtarhraða fóstura en ekki vegna styttri meðgöngu.

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Introduction

1 Adverse birth outcomes

Low birth weight (LBW) is widely used as an indicator of child health and is defined by the World Health Organization (WHO) as a birth weight below 2,500 grams in a live birth child. This definition is based on evidence from epidemiological studies suggesting that infants weighing less than 2,500 grams are approximately 20 times more likely to die than heavier babies [1, 2]. Birth weight is determined by two processes, i.e. duration of gestation and rate of fetal growth. Thus, infants can have birth weight below 2,500 grams either because they are born preterm (PB) or because they are born small for gestational age (SGA) due to intrauterine growth restriction (IUGR), or by a combination of both these factors [1, 3]. Although not all LBW deliveries are attributable to PB, this remains a major predictor of LBW in the industrialized part of the world. Preterm birth and IUGR are often studied together as tandem outcomes but because the etiology of these adverse outcomes may differ from one another, they will be discussed separately here below [4, 5].

Low birth weight and its antecedents IUGR and PB are major causes of infant mortality and morbidity in the world and have been associated with wide range of health problems that can stretch through childhood into adulthood. Those problems range from neurodevelopmental complications leading to emotional and cognitive problems [6-8], increased risk of schizophrenia [9, 10] as well as cerebral palsy [11]. Other conditions associated with LBW are respiratory distress and increased risk of cardiovascular and metabolic disease later in life [12, 13].

At the population level, the proportion of babies with LBW has been suggested to be an indicator of complex public-health problems, including long-term maternal malnutrition, ill health, hard work and poor health care in pregnancy. On an individual level, low birth weight is an important predictor of newborn health and survival. It is difficult to obtain an accurate estimate of the worldwide incidence of LBW, mainly because of limited access to reliable data for the developing countries. In a report published by WHO, the annual incidence of LBW in the year 2000 was estimated to be 15.5% of all births or more than 20 million births worldwide. The level of LBW in developing countries is more than double the level in industrialized countries or between 14-18% for Africa and Asia, respectively, against 6-8% in Europe and North-America, respectively [2]. Among the Nordic countries, Iceland had the

lowest rate of LBW deliveries in the year 2008 (3.8%) and Denmark and Norway the highest rate (5.3% and 5.1% respectively) [14].

Given these staggering numbers of adverse birth outcomes and their potentially serious long-term consequences, substantial effort has been made to understand the causes of IUGR and PB. However, despite intensive research the underlying etiologies of IUGR and PB remain unclear.

1.1 Low birth weight due to growth restriction in uterus

The American College of Obstetricians and Gynecologists has provided a definition of IUGR as a fetus that does not achieve their growth potential [15]. IUGR and its consequence SGA remain one of the main challenges in maternal care and are important public health problems. They are closely associated with fetal and perinatal mortality as well as morbidity. Frøen et al. reported a 52% percent of all stillbirths in Oslo during the time period 1986 – 1995 was associated with IUGR and and Richardus et al. found that 10% of perinatal mortality in ten European regions can be associated with IUGR [16-18].

The most commonly used definition of SGA is a birth weight below the 10th percentile for infants of the same gestational age, hence, by definition 10% of all infants are small for their gestational age. However, it is important to emphasize that some SGA infants may be constitutionally small but otherwise healthy and therefore not growth restricted. Others are smaller than expected and it is these individuals' small size that is of concern. It is recognized that fetal growth is influenced by factors such as ethnicity, infants' gender and maternal stature among other factors. In attempt to distinguish between SGA infants that are small but healthy and those who are pathologically small, researchers have developed customized fetal growth standards or individualized birth weight ratio for different sub-populations [19].

Intrauterine growth restriction can be categorized into groups, depending on when in pregnancy the restriction occurs. When substrate availability becomes scarce early in pregnancy, it may result in well-proportionate but growth-restricted infant. When negative fetal environment happens around the 30th week of pregnancy, a disproportionate SGA infant may be born. Lastly, negative factors occurring in the 3rd trimester may result in a fully grown but underweight SGA infant [20, 21].

1.1.1 Risk factors for intrauterine growth restriction

Intrauterine Growth Restriction is not a specific disease but rather combination of many fetal and maternal disorders. It is particularly important to ascertain the specific cause of growth failure in order to obtain the best possible outcome for the fetus and the mother. Several maternal, fetal and placental conditions have been associated with IUGR. Maternal demographic factors that have been associated with IUGR are following: Higher maternal age, unemployment, ethnicity and being single [22].

Maternal behavioral conditions include smoking, which causes a decrease in the blood flow to the utero-placental unit and thereby limiting the amount of substrates available to the fetus. Smoking during pregnancy may result in 150 – 300 grams decrease in fetal weight. Substance abuse (heroin, cocaine, alcohol) has also been associated with IUGR as well as some medications, among them warfarin and drug treatment for epilepsy [15, 19, 23, 24]. Insufficient maternal intake of nutrients may lead to IUGR if deprivation is severe [25] as well as low pre-pregnancy weight [3]. Of maternal medical risk factors the most relevant is vascular disease, for example hypertension, which results in decreased utero-placental perfusion. Hypertension is associated with 11 – 40% risk of IUGR, depending on the type of hypertension [19, 26]. Other maternal medical risk factors include conditions such as autoimmune diseases, pre-gestational diabetes etc.

Of fetal conditions related to IUGR, chromosome anomalies and congenital malformation are the most relevant, responsible for approximately 20% of IUGR fetuses. Multiple gestations are associated with IUGR and between 15-30% of twin pregnancies are growth restricted. Lastly, fetal infection may also lead to IUGR.

Placental risk factors are for example small placenta as well as abnormally formed placenta. Also, sometimes benign tumor in the placenta may cause IUGR. All these placental conditions are associated with impaired placental perfusion [15, 19, 21].

1.2 Preterm birth

Preterm birth is defined when infants are born less than 37 weeks of gestation. The precursors for PB are:

“1) Delivery for maternal or fetal indications, in which labour is induced or the infant is delivered by cesarean section; 2) spontaneous preterm labour with intact membranes; and 3) preterm premature rupture of the membranes (PPROM), irrespective of whether delivery is vaginal or by cesarean section.” [27]

Approximately 30-40% of PB is iatrogenic due to maternal or fetal complications, 25-30% follows PPROM and 40-50% follows spontaneous preterm birth [27]. The worldwide incidence of PB in 2005 was estimated to be 9.6% of all births or 12.9 million births. The highest rates were found in Africa and North-America, where 11.9% and 10.6% respectively of births were preterm. The rate of PB in Europe in 2008 was 6.2% with the lowest number in Sweden, Finland and Iceland (~5%) [14, 28].

Research indicates that spontaneous PB is a multifactorial syndrome, caused by different genetic, environmental and social factors but the interaction between these factors leading to PB is not clear [1, 29]. There is substantial evidence linking many maternal and fetal characteristics and PB. These include maternal demographic characteristics, nutritional status, present pregnancy characteristics, pregnancy history, psychological characteristics and adverse behavior such as smoking and heavy alcohol or substance misuse. Other factors known to play a role in the mechanism of PB, but will not be addressed in detail here, are biological and genetic markers as well infections and inflammation.

1.2.1 Risk factors for preterm birth

PB and IUGR have many common risk factors. Race and ethnicity have consistently been reported as risk factors for PB. Afro-Americans and Afro-Caribbean born in the US have been reported to have two-times higher risk of PB and four-time higher risk of extremely preterm birth (<28 weeks of gestation) than white women. This racial difference persists even when adjusting for other confounding factors [4, 30, 31].

The difference in risk of PB between African-Americans and other ethnic groups remains unexplained. It has been proposed that African-American women may be genetically different from women of Caucasian/Hispanic/Asian origin [32]. It has also been suggested that this increased risk of PB among African-Americans is caused by mothers' experience of racial discrimination and minority status [33, 34]. This hypothesis wins support when comparing the

incidence of PB among foreign-born African-American women in the US with African-American women who are US-born. Although yet higher than their Caucasian counterparts, African-American mothers who were born outside the US have significant lower risk of PB than black mothers, born in the US. It is therefore not likely that gene difference is the only explanation for increased risk of PB among African-Americans and probably the explanation lies in cultural, social and environmental context associated with race or ethnicity [32, 33].

Poverty is a consistently reported risk factor for PB across populations, time and various methods of quantifying social class and social status. A proposed explanation is higher exposure to negative life events in populations of poor people as well as fewer coping resorts and lack of social support. It is also known that poor communities are more exposed to environmental hazards and insecure neighborhoods. This all works together towards increased susceptibility of PB [35].

Maternal age has an effect on gestational length and the prevalence of PB. Older maternal age is associated with an increased prevalence of preexisting chronic diseases and medical problems during pregnancy as well as obstetric complications which are factors known to influence gestational length and the rate of PB. However, it is unclear if older maternal age is an independent risk factor for PB or if it is a risk indicator. Carolan et al. reported in a recent review an increased risk of adverse perinatal outcome among women aged 35-40 years old, a risk that was modest until 40 years of age or more [36, 37]. Similarly, mothers younger than 20 years old have increased risk of PB. To which degree this increase can be attributed to confounding factors such as family income, marital status, parity as well as other demographic factors, remains controversial. However, there is mounting evidence supporting the hypothesis that young maternal age is an individual risk factor for PB [38-40].

Being unmarried is a risk indicator for PB. It has been proposed that unmarried women lack social support and relationship stability, that they are exposed to risky behaviors or that they experience low social acceptance, all which might mediate the relationship between single marital status and PB [41].

Poor maternal nutritional status can lead to PB [42]. The suggested mechanisms are, among other, that 1) underweight women have decreased blood volume and reduced uterine blood flow and 2) underweight women may consume fewer vitamins and minerals which are associated with decreased blood flow and increased maternal infections leading to PB [27].

Tobacco use during pregnancy accounts for a slight increase in the risk of PB by mechanisms that still are not fully understood. It is known that tobacco contains thousands of

chemicals, among them nicotine and carbon monoxide that both are vasoconstrictors and can cause placental damage [43]. Use of other addictive drugs has been found to increase the risk of PB. No association has been found between low and moderate alcohol consumption and PB but heavy drinking can lead to PB [23].

Women with previous history of PB are at high risk of recurrent PB. This applies both to women with early spontaneous births as well as those with indicated PB. The underlying disorder causing indicated PB often tends to persist between pregnancies while the causes of recurring spontaneous PB are less known. Women with short interpregnancy intervals have increased risk of PB than women with longer time between their pregnancies. One plausible explanation is that the uterus takes time to return to its normal state. It could also be that maternal stores of essential nutritional compounds have not been restored from previous pregnancy [27].

There are several maternal medical disorders that have been associated with PB. Two of the most relevant are hypertension and diabetes. Hypertension during pregnancy (chronic, gestational and preeclampsia) is the most common pregnancy-related disorder in western countries with estimated incidence ranging from 8% - 10% [44]. About 70% of women diagnosed with hypertension during pregnancy will have gestational hypertension-preeclampsia which can lead to growth restriction in uterus, indicated or spontaneous preterm birth or, in severe cases, to perinatal death. Mild to moderate hypertension is associated with 33% increased risk for PB. This risk becomes higher if the hypertension is severe or up to 60-70%. Hypertension-preeclampsia is more frequent in socially disadvantaged women, in older women and African-Americans [26]. The rate of preeclampsia increased by 40% between 1990 and 1999 and this increase is probably the results of a rise in the number of older mothers and multiple births [44].

Pre-existing diabetes (type 1 & 2) and gestational diabetes is the second most common medical disorder during pregnancy and is an increasing problem in obstetric practice. Increasing obesity and greater maternal age are leading to an increase in the incidence of pre-gestational type 2 diabetes and gestational diabetes with the incidence ranging from 3% - 13%, depending on risk factors. Diabetic women face number of adverse birth outcomes, for example preeclampsia, which often leads to indicated caesarean section. Risks for the fetus include malformation, spontaneous abortion, stillbirth, neonatal death, macrosomia and intrauterine growth retardation. The risk of gestational diabetes increases with obesity, maternal age, ethnicity and a family history of diabetes [45, 46].

1.3 Stress and birth outcomes – overview of literature

Cohen et al. have defined stress, as follows: “*when environmental demands [internal or external; real or imagined] tax or exceed the adaptive capacity of an organism, resulting in psychological and biological changes that may place persons at risk for disease*” [47]. Stress is often divided into two subcategories: acute stress and chronic stress. Acute stress is a psychological condition arising as a reaction to an immediate threat, shock or trauma. This type of stress is typically resolved by the stress mechanism of the human body. Chronic stress evolves when a stressor is present over long periods of time or if a person is under constant adverse stimuli. This results in constant arousal of the stress mechanism and is thought to play major role in the development of psychological and somatic illness.

The effects of stressors on fetal development and birth outcomes have been a subject for research for many decades and have yielded somewhat conflicting results [5]. Here below, an overview of studies conducted in this field is provided; the studies will be reviewed in two sections depending on the type of stressor, i.e. acute vs. chronic stressor.

1.3.1 Acute stress

The terrorist attacks on the World Trade Center (WTC) on September 11th 2001 were an example of an acute stressor. It was a source of massive psychological trauma and created an acute environmental disaster caused by the burning fuel of the airplane and the collapse of the buildings. Several studies have been conducted on the effect of this extreme trauma on the health of pregnant women and birth outcomes, producing results that are, yet again, inconclusive.

Some studies have reported an increased risk of LBW and PB, shorter gestational length and decreased birth weight as well as shorter length of infants born, among women who were in proximity of the WTC during the terrorist attacks [48-53]. Other studies have either found no association between the WTC attacks and birth outcomes [54, 55] or directly the opposite effect [56, 57]. El-Sayed et al. report a lower risk of very low birth weight and PB among Arab-American women in Michigan after the terrorist attack compared with before [55] and Rich-Edwards et al. report a decreased risk of preterm birth among women giving birth in Boston following the 9/11 terrorist attack [56]. Engel et al. report a significant increase in gestational length in highly exposed women with posttraumatic stress symptomatology and moderate depression [57]. Lastly, Endara et al. conducted a large historical cohort study, including infants born to all active-duty military US families and found no association between the 9/11 attack and adverse birth outcomes [54]. It is difficult to draw any

conclusions based on these contradicting results and further examination is needed. Furthermore, given that the attacks affected birth outcomes to worse, it is difficult to determine whether these adverse birth outcomes are due to mechanisms of stress or environmental pollutants.

Natural disasters such as earthquakes, floods and hurricanes are other examples of acute stressors which, surprisingly, have not been examined in details. Few studies on these topics, report an increased risk of adverse birth outcomes among exposed women, with the risk being highest among those with the most intensive experience [58-61].

1.3.2 Chronic stress

While earlier studies focused on the effect of major shocks on birth outcomes, more recent research has examined the role of chronic stressors in the same context and numerous studies have been conducted examining the effect of wide range of chronic stressors on infant health. Among chronic stressors examined are racial distress, low socio-economic status and other psychosocial stressors such as anxiety, depression, unemployment, neighborhood, household disadvantages and relationship status. It is widely recognized that poor parental education, low social status and African-American ethnicity are positively associated with LBW and PB [35, 62-68]. There is more uncertainty to which degree other psychosocial stressors affect the gestational process.

Parlberg et al. conducted an extensive review of literature involving chronic stressors and various adverse birth outcomes, i.e. infants' relative birth weight, low birth weight, gestational length and preterm birth, Apgar scores outcomes, congenital malformation and perinatal death. Their conclusion was that a positive association was present and it was strongest when multiple exposures interact to contribute to adverse birth outcome [69].

1.3.3 The perception and timing of stress in pregnancy

In studies focusing on stressful life events, two factors have emerged as relevant to the risk of PB and LBW – 1) the timing of the stressor and 2) women's perception of it.

Some studies have indicated that women are most vulnerable to stressful life events occurring in the 1st trimester of the pregnancy. It has moreover been reported that women, experiencing a stressful life event during the year before the pregnancy have increased risk of giving birth to infants who were small for gestational age or born preterm [70-72]. Glynn et al. showed that among pregnant women exposed to earthquake, only those who experienced it during the first trimester showed significant association with PB [73]. This same pattern also

appeared among pregnant women living in close proximity to WTC during the 9/11 terrorist attack, only those in their 1st trimester showed significant association with PB [51]. By contrast, Hedegaard et al. reported that stressful life event happening before the 30th week of gestation was associated with shorter gestational age but not if the life event happened before week 16 [74].

Studies of life events have indicated that an occurrence of life event assessed as highly stressful by women is associated with adverse birth outcomes, even though that particular event in it self is not. Hedegaard et al. reported a positive association between PB and adverse life events is the events were appraised as highly stressful by women. This association was not seen when total scores of life events was used as independent variable instead of the women's subjective assessment [74]. This indicates that women's experience of life events during pregnancy seems to be relevant in predicting PB and LBW. Lu et al. reported significant racial-ethnic disparities in the experience of stressful life events before and during pregnancy but these disparities do not contribute significantly to the racial-ethnic disparities observed in PB [34].

1.3.4 Pathophysiological mechanisms

The following section will focus on the biological stress response relevant for fetal development and birth process.

First it is relevant to mention that stressful conditions can promote adverse behavior such as smoking and alcohol- or drug abuse which are, as discussed previously, recognized risk factors for IUGR and PB. Thus, adverse health behavior may act as mediator between stress response and IUGR and PB [75].

However, a direct effect of stressful stimulation on pregnancy has been hypothesized through following possible pathophysiological mechanism: 1) via the role of the stress hormones and 2) via immunologic processes, which are known to be under the influence of psychosocial factors via neural and endocrine mediating pathways [69].

Stress hormones and adverse birth outcomes

In non-pregnant state the hypothalamic-pituitary-adrenal axis (HPA) modulates the response to an external stressor with the corticotrophin-releasing hormone (CRH) acting as the mediator for the stress response. When an individual perceives a stressor, CRH is secreted from hypothalamus and stimulates the release of adreno-corticotropin hormone (ACTH) by the pituitary gland. ACTH is transported through the systematic circulation to the adrenal gland where it stimulates the release of cortisol, a primary stress hormone. Cortisol then shuts down the secretion of ACTH and CRH through negative feedback loop and homeostasis is reestablished [5, 69]. When stress becomes chronic or excessive these adaptive mechanisms may fail, leading to chronic elevation of cortisol and, possibly, a disease. The adaptive capacity differs markedly between individuals and the amount of stress one person can cope with may be too much for another to handle. An individual's unique characteristics and life circumstances, there among coping skills, personality, social status, social support etc., can affect the stress appraisal and the stress response of the body [76].

During pregnancy, cortisol stimulates CRH gene expression in the placenta causing a positive feedback loop between the adrenal glands and the placenta. This results in progressive increase in CRH levels during pregnancy. Furthermore, there is an increase in CRH-binding protein, limiting the amount of free CRH during pregnancy. Thus, CRH is thought to play a central role in the process of birth and parturition, possible by keeping the uterus in relaxed state. Studies have shown that women at risk for PB have increased levels of

CRH and decreased levels of CRH-binding protein, resulting in increased amount of free CRH. It has also been documented that increase in the stress hormones (ACTH and cortisol) in 1st and 2nd trimester of pregnancy predicts a rise of CRH [5, 77]. To summarize, it appears that CRH has counteractive role in pregnancy, on one hand it is a necessary cofactor that leads to healthy pregnancy and term labor but on the other hand, once threshold level has been reached, CRH plays a significant role in PB.

Increased level of stress hormones during pregnancy results in a decrease in the blood flow to the uterus, thereby limiting the substrates delivered to the fetus during pregnancy and possibly causing IUGR. Recent studies indicate that maternal smoking is associated with an increase in the level of stress hormones. Fetal exposure to stress hormones, particularly cortisol, can result in reduced birth weight [5].

Immunologic factors and preterm birth

As discussed above, a stressful stimuli results in release of stress hormones. Increased level of the stress hormones, i.e. catecholamines and cortisol can suppress the immune system, resulting in increased vulnerability to infections. Infections can be located in the fetal membranes, placenta, within the amniotic fluid or in the umbilical cord [78]. Infections during pregnancy are associated with preterm premature rupture of membranes (PPROM) which can lead to PB. Preeclampsia has also been associated with alteration in immunologic function. In the case of immunologic adaptation, a process on a cellular level is initiated causing endothelial damage, which forms a part of the preeclamptic process [69].

Despite intensive effort, studies conducted to shed light on the association between acute or chronic stress and adverse birth outcomes have failed to produce consistent results and interventions designed to reduce the incidence of adverse birth outcomes have not proved efficient. There is, however, a strong biological plausibility linking stress to PB and LBW and therefore researchers are seeking to overcome a number of methodological problems that could be masking the true association. Among aforementioned problems are: defect methods for measurements of stress and individuals' coping mechanisms, use of different outcome assessments; for example use of conventional instead of customized birth weight standards or not distancing between different types of preterm birth.

2 Economic crisis and public health

The question if and then to what extent economic recessions affect public health has been examined extensively for several decades and research conducted to sheer light on this association have yielded mixed results. Many investigators have expressed their concerns about possible adverse health effects of the current recession, mostly through increased unemployment rate and its effect on psychiatric disorders and adverse health behavior [79, 80].

Brenner's studies from the 1970's lend support to the hypothesis that an economic downturn has negative impact on people's health status, measured as overall mortality as well as mortality due to specific causes such as cardiovascular disease, suicides and homicides [81-83]. Many later studies, designed to replicate Brenner's results, have failed to obtain similar results [84-87]. However, a recent study conducted in Brazil found an increase in mortality rates during economic recession. The results suggest that as macroeconomic conditions improved, increasing employment rates, there was a decrease in the mortality rate [88].

Other analysts have found that economic recessions are followed with a decrease in mortality rates in high income countries. A suggested explanation of these results is that temporary decreases in the opportunity cost of time may lead to healthier lifestyle, such as increased physical activity which may lead to decreased obesity. The associated income effects may similarly decrease use of tobacco and alcohol [89, 90]. Furthermore, it has been suggested that the increased time spent with families and friends, resulting in improved social network, may lead to health gains.

These contradicting findings make the net effect of economic recessions difficult to estimate and can probably be explained by different methods used to evaluate recessions. The former view of negative impact of recessions on health is mostly supported by studies examining the association between involuntary unemployment and health on individual level [91-95], whereas the latter view – “that recessions are good for population health” - is supported with studies where aggregate data is used to determine the effect of economic fluctuations on health [89, 90]. Some of the differences in findings from these two traditions may be related to differential use of lag-time; etiologically, several serious health endpoints will not be apparent until considerable time with exposure to economic hardships. Also, while it is conceivable that average population health levels improves somewhat, some vulnerable subpopulations may at the same time suffer great health losses.

2.1 Plausible mechanism connecting economic crisis and birth outcomes

Zilko et. al have presented an overview of mechanisms connecting recessions with the process of gestation and birth outcomes (figure 1)[96]. The empirical evidence supporting these mechanisms is reviewed below.

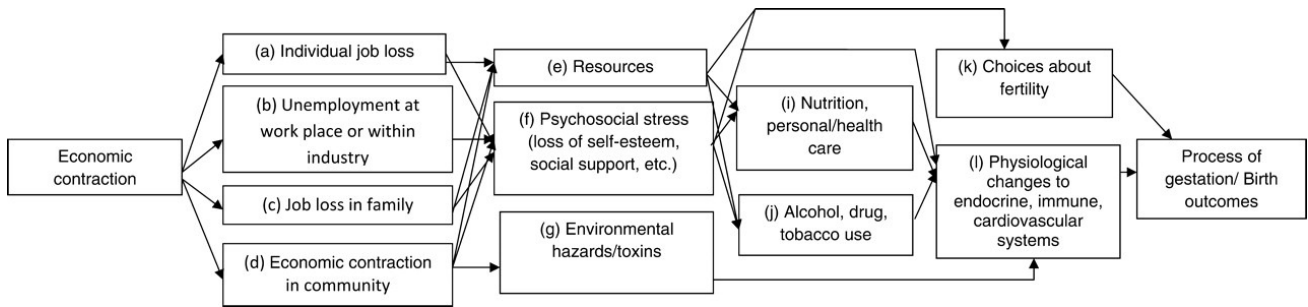


Figure 1: Plausible mechanisms connecting economic contraction to gestational outcomes.

On a macro-level, economic downturns lead to a general contraction of economic activity in communities and elevated unemployment rates. A subsequent decrease in governmental resources typically results in cuts in public services such as the health care, educational and social systems [97, 98]. At the individual level, economic contractions can have heterogeneous effects. Lay-offs at work places is one manifestation that leads to loss of means for those affected. Other members of families in which one loses a job are also influenced due to loss of resources. Those who remain employed may accept cuts in wages or an increase in work load in order to maintain their jobs. Being unemployed is associated with worse mental health [99] and an increase in psychosocial stress [100], which, together with less resources, may promote adverse health behavior such as smoking, alcohol or substance misuse. Psychosocial stress and loss of resources may also lead to worsened nutritional intake and decrease in personal care [79]. The literature indicates that pregnant women are a vulnerable group, particularly those in the 1st trimester when experiencing an adverse event [70, 73]. Abovementioned factors have been associated with physiological changes to the endocrine-, immune- and cardiovascular systems which, as discussed above, may lead to shortened gestation and/or IUGR.

2.2 The economic crisis in Iceland

On October 6th 2008 Prime Minister at that time, Geir H. Haarde, appeared on television and addressed the nation in live broadcast to appraise the impending financial crisis. The speech was unusually frank and emotional and came as a shock for the majority of Icelanders. The same afternoon the Icelandic parliament passed emergency legislation enabling the government to intervene in Iceland's financial system and FME, the Financial Supervisory Authority in Iceland, took wide-ranging authority over its three largest banks; Kaupþing, Landsbankinn and Glitnir. This day has widely been viewed as the beginning of the severe economic crisis in Iceland. This started a course of events that have resulted in a number of unforeseen consequences, among them the UK government's decision to invoke anti-terrorism legislation to freeze the Landsbankinn assets, emergency funding from the International Monetary fund as well as massive protests against the government with related political instability resulting in a cabinet change in February 2009.

In order to sheer light on the magnitude of this economic collapse and to put it into perspective it is relevant to mention that the Icelandic banking sector expanded dramatically in the year's preceding the collapse. At the end of June 2008 the combined assets of the above-mentioned three banks were 14 times larger than the GDP of Iceland. The Icelandic banking system was in fact one of the largest in the world in relation to GDP [101].

During the crisis, a large portion of the populace lost their savings and others were left with serious debt. Families had taken advantage of cheap credit to buy houses and consequently found themselves trapped in negative equity. Since January 2008 the cost-of-living index in Iceland has increased by 28.7% and the purchasing power has decreased by 15.5% from 2008 to 2009 [102].

Unemployment rate has gone from being 2.3% in the 1st quarter of 2008 to 7.4% in 4th quarter 2010. The unemployment rate peaked in the 2nd quarter 2009 when it was 9.1%. The unemployment rate is far from uniformly distributed across age, with the highest rate (21.9% in 2nd quarter 2009) among young people in the age group 16 – 24 year old [103]. An unemployment increase of this magnitude is a rare event in EU countries.

With this in mind it is not unreasonable to assume that this rapid and largely unforeseen collapse of the Icelandic economy has been a source of great psychological stress in the general population. In fact, recent studies indicate that psychological stress has indeed increased, particularly among women [104].

The aim of the study

The rapid and largely unforeseen collapse of the Icelandic economy represents a potentially important stressor that may adversely affect the development of the fetus. With this in mind it is relevant to draw upon today's circumstances and learn how an economic recession affects birth outcomes.

In this study we will explore the incidence of adverse birth outcomes in the time of crisis. The research question addressed in this study is threefold: Are women giving birth at the time of crisis at higher risk of having LBW, SGA or PB infants than women giving birth in the two preceding years? Assuming there is an increased risk, are there subgroups within the study population who are more affected by the crisis than others? Lastly, we will look at the development of the risk over time following the economic collapse in order to see when potential increase occurred.

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Risks of low birth weight, small-for-gestational age and preterm births following the economic collapse in Iceland

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Abstract

Objective: Infants born small for gestational age (SGA) and preterm have increased rates of perinatal morbidity and mortality. Stressful events have been suggested as potential contributors to preterm birth (PB) and low birth weight (LBW). We studied the effect of the 2008 national economic collapse in Iceland on the risk of these adverse birth outcomes.

Study design: The study population constituted all Icelandic women giving birth to live-born singletons from January 1st 2006 to December 31st 2009. LBW infants were defined as those weighing <2500 grams at birth, PB infants as those born before 37 weeks of gestation and SGA as those with a birth weight for gestational age more than 2 SD below the mean according to the Swedish fetal growth curve. We used logistic regression analysis to estimate odds ratios [OR] and corresponding 95 percent confidence intervals [95% CI] of adverse birth outcomes by exposure to calendar time of the economic crisis, i.e. after October 6th 2008.

Results: Compared to the preceding period, we observed a short-term increase in LBW deliveries following the economic collapse (aOR=1.24, 95% CI [1.02, 1.52]), particularly among children born to women younger than 25 years (aOR=1.85, 95% CI [1.25, 2.72]) and mothers not working (aOR=1.59, 95% CI [1.10, 2.31]). Similarly, following the economic collapse, we found a trend towards higher incidence of SGA births (aOR=1.14, 95% CI [0.86, 1.51]) particularly among children born to women younger than 25 years (aOR=1.85, 95% CI [1.08, 3.19]) and to women not working (aOR=1.84, 95% CI [1.09, 3.10]). No change in risk of PB was observed.

Conclusion: The results suggest a short term increase in risk of low birth weight following the dramatic collapse of the Icelandic national economy. The increase in LBW seems to be driven by reduced fetal growth rate rather than shorter gestation.

Introduction

Infants born small for gestational age or preterm have increased risks of perinatal morbidity and mortality [105, 106] and of somatic diseases that can last throughout childhood and into adulthood [13, 107].

It is a common belief that emotions, behavior and environment of a pregnant woman can affect fetal development and numerous studies have been performed to test this hypothesis. A number of studies have addressed associations between emotional and stressful life events during the prenatal period and adverse birth outcomes. However, the results of these studies are inconclusive, with some studies reporting that adverse life events increase risks of poor pregnancy outcomes [48, 51, 58-60, 71, 72, 74] while others find either no association [54, 108] or directly the opposite [55]. Whether economic crisis during the prenatal period have adverse effects on offspring health has been less investigated. Deheer and Llers-Muney reported a reduced incidence of adverse birth outcomes during periods of high unemployment [109]. Other studies have found either null associations [85, 86] or higher risks of low birth weight and neonatal mortality following recessions or involuntary unemployment [83, 110, 111].

On October 6th 2008 the Icelandic government took wide-ranging authority over its three largest banks and the prime minister addressed the nation in a dramatic manner the advent of this unusually swift and a severe national economic crisis. The largely unforeseen collapse of the Icelandic economy as well as the rapid rise in unemployment and household debts represent a powerful stressor that may adversely affect birth outcomes. Using the nationwide medical birth registry, our aim was to study the effect of the 2008 economic collapse in Iceland on infant health, as measured by low-birth weight, preterm birth and small-for-gestational age.

Materials and Methods

Population

All Icelandic women registered in the National Icelandic Birth Registry from January 1st 2006 to December 31st 2009 (N=16,616) were considered. Women were excluded from the study if they had multiple pregnancies during the study period (n=298) or if they had experienced stillbirth (n=47), leaving a total of 16,271 eligible women in the study.

Outcome assessment

Low birth weight (LBW) infants were classified as those weighing less than 2,500 grams at birth. Preterm birth (PB) was defined as delivery before 37 completed gestational weeks (259 days of gestation). In 16,228 births (>99.9%), length of gestation was based on ultrasound measurement before the 21st week of gestation. In 7 pregnancies, gestational age could be estimated on the basis of last menstrual period, whereas it could not be determined for 8 cases. Small-for-gestational age (SGA), a proxy for intrauterine growth restriction, was defined as infants with birth weight more than 2 standard deviations (SD) below the mean for gestational age, according to the Swedish fetal growth curve described by Marsál et al. [112], which has been shown to be applicable for Icelandic fetuses [113]. Fetal growth rate index (Z scores) was also assessed by using this method [112].

Explanatory variables

The study period was dichotomized with pre-crisis period (“unexposed”) spanning from January 1st 2006 to October 5th 2008 and post-crisis period (“exposed”) spanning from October 6th 2008 to December 31st 2009. Infants born later than October 5th 2008 were considered exposed as they were born during times of economic crisis and infants born from January 1st 2006 up until the economic collapse were used as a referent group. The pre- and post-crisis groups will hereafter be referred to as the unexposed and the exposed group, respectively.

Potential covariates

Information on covariates was obtained from the National Icelandic Birth Registry. Maternal characteristics obtained from the registry were: place of delivery; maternal age at delivery; parity (nulli-, primi- and multiparous); relationship status (mother cohabitating with father or not); employment status (employed or not employed (student/housewife/unemployed/on disablement benefit)); residence (living in the capital area or not); pregnancy-related diseases known to influence fetal growth with ICD-10 classification numbers O10-O14 (hypertension; pre-existing and pregnancy-induced - preeclampsia) and O24.0 -24.9 (diabetes mellitus; pre-existing and gestational). Obstetric information obtained was: mode of delivery (vaginal or cesarean delivery), infants' sex, Apgar score at 5 minutes, vaginal induction of delivery (O83.8), congenital malformations and chromosomal abnormalities (ICD-codes Q00-99) and early neonatal death (within 7 days from birth). In order to account for seasonal variation of birth weight, the years were divided into four seasons and births occurring in the same season were grouped together in the unexposed and exposed groups, respectively.

Statistical analysis

We calculated descriptive statistics for all maternal and obstetric characteristics as well as for LBW, PB and SGA, contrasting frequencies before and after the economic collapse. Differences in characteristics by exposure groups were explored using the Chi-square test for categorical variables, independent sample t-test was used for maternal age and linear regression analysis, adjusted for maternal age, parity and seasonality, for gestational length and birth weight. One-way ANOVA test with post-hoc Tukey's test was conducted to assess the homogeneity of birth weight between seasons. Logistic regression analysis was used to calculate adjusted odds ratios (aOR) and their 95% confidence intervals [CI's] for LBW, PB and SGA in the exposed period. In model I, adjustments were made for variables assessed as possible confounders: maternal age, parity and seasonality. In model II, we explore whether possible increased risks of adverse birth outcomes were mediated by other maternal factors or diseases during pregnancy all which, in fact, may have been influenced by the crisis. In model II, we therefore also adjusted for: relationship status, residence, employment status, hypertension and diabetes. Analysis involving LBW and PB were also adjusted for infant's sex in model II. We used linear regression models to estimate changes in fetal growth rate index across exposure categories.

To further explore whether associations between PB, SGA and LBW differed depending on when in gestation the collapse hit, we divided the study period into intervals of three months and compared those in 2008 and 2009 with same time intervals during preceding two years. Each time interval in 2008 and 2009 averaged 1,050 births and comparison groups, combining 2006 and 2007, averaged 1,974 births.

Additional analysis was conducted to examine the effect of the shock on fetuses that were in uterus on the day of the collapse. The exposed group consisted only of those women who were pregnant on October 6th 2008. Women, pregnant on same day in the two preceding years, were considered unexposed. Similar analysis was carried out to examine the effect of the crisis on women that became pregnant during the post-crisis period and gave birth in the last 6-7 months of 2009. Reference group consisted of women who became pregnant after October 6th 2006 and gave birth the following year.

In order to detect a possible time-trend in LBW, SGA and PB we used logistic regression analysis to calculate the odds of each birth outcome, operated in calendar days, separately for each time period. This regression model was adjusted for maternal age, parity and seasonality.

Ethical considerations

The study was approved by the Icelandic National Bioethics Committee (VSNb2010050014/03.7), the Data Protection Authority (2010050499LSL/--) and the Directorate of Health (2010050296/5.6.1/HBS/hbs).

Results

Among all 16,271 infants; 11,111 (68%) were in the unexposed group and 5,160 (32%) were in the exposed group. Table 1a and 1b present the maternal and obstetric characteristics by exposure status. Following the economic collapse, we observed a statistically significant increase in maternal age as well as a tendency towards higher parity. Compared to the pre-crisis period, the mothers giving birth following the economic collapse were more likely to be single, not working and suffer from pregnancy-induced hypertension and gestational diabetes. The infants born in the period of the economic crisis weighted on average 28 grams less than infants in the reference group (table 1b). There was also a small but statistically significant difference in mean gestational length between births in the exposed and unexposed periods. No differences were observed with respect to maternal residence, mode of delivery, sex of infants, Apgar score at 5 minutes, congenital malformation or early neonatal death. Post-hoc Tukey's test did show a statistically significant difference between the seasonal variation of birth weight in the pre-crisis period but not in post-crisis period.

Two point six percent of infants were born with low birth weight (<2,500 grams) during the study period, and the corresponding rates before and after the collapse were 2.5 % and 3.0%, respectively. Table 2 shows the results for multivariate logistic regression analysis. When adjusting for maternal age, parity and seasonality (model I) we observed a statistically significant increase in the odds of LBW during the post-crisis period (aOR=1.26, 95% CI [1.02, 1.52]). When we further adjusted for other variables (model II) this difference became statistically insignificant (aOR=1.16, 95% CI [0.94, 1.43]).

Four and a half percent of infants were born preterm during the study period, and corresponding rates were 4.3% before and 4.6% after the economic collapse. No statistically significant association was observed between the risk of PB and being born after the collapse.

One point four percent of all infants were assessed as SGA; before the crises 1.4% were SGA and after the crises, 1.5% were SGA. When applying logistic regression analysis, we found no significant association between time of crisis and risk of SGA. Additional analysis was conducted to estimate the change in fetal growth rate index between pre- and post crisis groups. Infants, born in time of crisis, had a decreased rate of fetal growth when compared to the reference group ($\beta = -0.004$; 95% CI [-0.009, 0.000]). This decrease was particularly distinct for women giving birth in the time period April – June 2009 ($\beta = -0.015$, 95% CI [-0.025, -0.006]).

Figure 1 presents results from logistic regressions of LBW and SGA around the economic collapse in the three-month intervals, 3 before the economic collapse (January 1st – October 5th 2008) and 5 after (October 6th 2008 - December 31st 2009), using identical calendar times from the two preceding years as reference periods. After the economic collapse, we observed a statistically significant increased odds of LBW (aOR=1.70, 95% CI [1.11, 2.59]) in the interval April – June 2009 which is 6-9 months after the beginning of the crisis (figure 1a). A tendency towards increased odds of SGA was observed in the intervals January – March 2009 and April – June 2009, which is 3-6 months and 6-9 months after the beginning of the crisis (figure 1b). There were no associations observed between PB and stressors of the crisis in any of the three months intervals (figure 1c).

This pattern is coherent to the results obtained from the analysis of fetuses' in-uterus on the day of the collapse, where a tendency towards increased risk of LBW (aOR=1.25, 95% CI [0.95, 1.66]) and SGA (aOR=1.30, 95% CI [0.90, 1.88]) deliveries was observed but not in PB (aOR=1.05, 95% CI [0.84, 1.31]). Infants, conceived during the crisis, were not at increased risk of LBW, SGA or PB; ((aOR=1.06, 95% CI [0.75, 1.48]), (aOR=0.94, 95% CI [0.56, 1.58]), (aOR=1.07, 95% CI [0.81, 1.40]), respectively).

Table 3 presents multivariate adjusted odds ratios of LBW and SGA during the crisis period stratified by potential effect modifiers. If the mothers were younger than 25 years, there were statistically significant increased odds of giving birth to LBW and SGA infants in the exposed group compared with the unexposed group (aOR=1.85, 95% CI [1.25, 2.72]; aOR=1.85, 95% CI [1.08, 3.19], respectively). Similarly, if mothers were not working, corresponding risks among exposed women were increased (aOR=1.59, 95% CI [1.10, 2.31]; aOR=1.84, 95% CI [1.09, 3.10], respectively). Exposed mothers living outside the capital area had also statistically significant increased odds of having LBW infant compared to unexposed group (aOR=1.54, 95% CI [1.08, 2.19]).

Finally, analysis of time-trends in LBW, SGA and PB did not reveal a statistically significant trend for any of these adverse birth outcomes, in either of the two time periods (data not shown).

Discussion

The results from this nationwide study indicate a decrease in mean birth weight as well as an increased rate of LBW deliveries in Iceland in the months following the economic collapse. This effect was mainly observed among relatively young mothers and mothers without a job. Women who were in their 1st trimester of pregnancy at the advent of the swift and dramatic collapse seemed mostly affected which is in accordance with findings of Glynn et al. and Lederman et al. in their studies of major adverse life events effects on birth outcomes [51, 73]. Although, limited by small numbers, our findings suggest that the increase in LBW is driven by intrauterine growth restriction rather than shorter gestation.

Interestingly, the increase in LBW and SGA births during the crisis period was considerable among mothers in a vulnerable situation, namely young mothers and those without employment. Our findings are in line with studies that have assessed the impact of age and unemployment on birth outcomes. Young maternal age has been found to be an independent risk factor for adverse birth outcomes in several studies, with the strongest effect among mothers younger than 20 years old [38-40]. Young mothers without established careers or independent economies may be a particularly vulnerable group during times of hardships. Indeed, unemployment rates have been highest in this age group in Iceland during the crisis and rose up to 21% in the 2nd quarter 2009 and 2010 [103].

The role of unemployment in the causal relation has been of more controversy in previous studies. Dooley and Prause report a decrease in birth weight of infants born to women who shifted from adequate employment to underemployment during pregnancy [111]. Furthermore, Catalano et al. found increased risk of very LBW infants among parents where the father was unemployed [114] and lastly, Jansen et al. found a decrease in mean birth weight among offspring of students and women receiving disability benefits [115].

It should be noted that the “not working” group is very heterogeneous, consisting of unemployed, invalids, housewives and students. Therefore, this grouping may not be comparable to other studies examining the effect of unemployment on birth outcomes. However, the two largest groups were students and it can be argued that being a student in Iceland nowadays may be a proxy for unemployment, as many of those who lost their jobs during the crisis subsequently went to school.

A positive association was found between rurality and LBW. Since the impact of the crisis was in the beginning most severe for inhabitants living in the capital area and nearby areas, the opposite was expected. A possible explanation may be that we included in the rural area

category a relatively densely populated area in the south-west part of Iceland, Suðurnes, which was hit especially hard by the economic crisis. Unemployment rate in Suðurnes was 13-14% in 2009, the highest in Iceland. Also, some studies have in agreement to our results found increased risk of LBW infants and PB among women that live in rural and economically depressed counties [116, 117].

Hypertension has been identified as a risk factor for LBW, SGA and PB [15, 27]. The incidence of hypertension diagnosed during pregnancy did increase following the collapse but when hypertension was added to the models, the results did not indicate that the observed increases in LBW and SGA were mediated via hypertension. Several other mechanisms may explain the observed association between the economic recession and increase in LBW/SGA. The economic collapse may have increased the stress levels among pregnant women causing direct physiological changes to the endocrine, immune and cardiovascular systems; changes that may affect the process of gestation to the worse [5, 77]. Furthermore, it is well recognized that stressful conditions, such as income shocks, may promote adverse health behaviors, e.g. smoking, drinking etc. [75, 118] thus acting as a mediator between the stress caused by the economic collapse and the observed increase in LBW/SGA.

Validity

This study leverages the National Medical Birth Registry to accomplish a population-based cohort study of all pregnant Icelandic women giving birth in Iceland in a four year time period. A multitude of information on the mother and child has been systematically collected to the registry since 1973 and this collection is totally independent of exposure level, i.e. times of economic recession. Several measures were taken in order to further enhance the internal validity of this study. In order to make the cohort homogenous with regard to birth weight and length of gestation, we excluded all stillbirths and multiple gestations. Furthermore, our dataset included only Icelandic women, as the literature indicates that risks of IUGR and PB may differ by ethnicity. The majority of pregnant women undertake ultrasound scanning around the 20th week of pregnancy and therefore the measurement of gestational length is highly accurate. Almost all (99%) births occur in hospitals or at local health clinics, resulting in accurate measurement of birth weight. The richness of information in the Medical Birth Registry allows us to control for other major confounding factors, although we finally decided that changes occurring in most covariates (cohabitation,

working–status, diabetes and hypertension) may actually be a consequence of the economic collapse and therefore in the causal chain to LBW/SGA.

A limitation of this study is the lack of information on maternal smoking, alcohol, and nutritional habits during pregnancy. Use of tobacco during pregnancy is a well known and recognized risk factor for LBW and IUGR [15, 19, 24]. Furthermore, some researchers have suggested that stressful circumstances are often alleviated by adverse health behavior, such as smoking [75, 118]. Therefore, it is well possible that the prevalence of smoking or other unhealthy behaviors has increased during the economic collapse and that change in smoking behavior influenced the associations between the economic crisis and risks of LBW and SGA births. Further, we did not have information on pre-pregnancy maternal weight. Low pre-pregnancy weight is associated with both SGA and LBW and high pre-pregnancy weight is associated with pregnancy-induced hypertensive diseases-preeclampsia which often leads to SGA and PB [3, 45]. It is well recognized that maternal weight has been increasing in Iceland in the last decade thus we cannot rule out that the observed increase in LBW and SGA is attributable to increased maternal weight. However, our separate trend analysis before and after the economic collapse indicated a somewhat stable rate of LBW both before and after the economic collapse. Nevertheless, further studies are needed to address if the effect of the economic crisis on LBW is mediated through altered behavior, exposure to heightened levels of stress hormones or both.

Lastly, the shortage of a contemporaneous comparison group is a potential threat to the validity of this study. It should further be noted that the pre- and post crisis periods do not have identical calendar length which may have affected the results. However, trend analysis indicated a stable rate of LBW and all statistical models were adjusted for seasonality.

Conclusion / Implication

Taken together, the results of this study add important knowledge on how birth outcomes are affected when the economy of a whole nation collapses practically overnight. Our results indicate that economic melt down is an important stressor which increases the risk of LBW deliveries, especially when happening in the 1st trimester of pregnancy. The increase in LBW seemed not driven by shortened gestation but rather growth restriction in uterus. The crisis appeared to have the largest effect on younger women (<25 years) and women who were not employed.

These findings suggest that the effect on LBW was short lived; however, further studies with longer follow-up are needed for definite conclusion, particularly to observe whether the effect for young and vulnerable women is persistent. The findings have implications for public health practice and clinical management of pregnant women, particularly young women and women in a vulnerable situation at the labor market.

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Table 1a – Maternal characteristics during the study period, before and after Oct 6th 2008

Maternal characteristics	Category of characteristics	Precrisis (N=11,111)		Postcrisis (N=5,160)		p-value*
		Births, n	Births, %	Births, n	Births, %	
Mean age (SD)		29.01 (5.55)		29.24 (5.54)		0.016**
Age (year)	<25	2,454	22.09	1,055	20.45	0.036**
	25-34	6,734	60.61	3,160	61.24	
	≥35	1,923	17.31	945	18.31	
Parity	nulliparous	4,324	38.92	1,966	38.10	0.072
	primiparous	3,929	35.36	1,779	34.48	
	multiparous	2,858	25.72	1,415	27.41	
Relationship status [‡]	Cohabiting with father	9,422	86.38	4,182	84.18	<0.001***
	Single	1,485	13.62	786	15.82	
Place of residence [¥]	Rural	3,799	34.53	1,715	33.27	0.119
	Urban	7,203	65.47	3,438	66.73	
Employment status ^β	Working	8,247	75.23	3,783	74.48	0.312
	Not working	2,716	24.77	1,296	25.52	
Diabetes	No	10,783	97.05	4,953	95.99	0.001***
	Pre-existing	47	0.43	21	0.42	
	Gestational diabetes	281	2.53	186	3.60	
Hypertension	No	10,290	92.61	4,721	91.49	0.045**
	Pre-existing	151	1.36	82	1.59	
	Pregnancy-induced-preeclampsia	670	6.03	357	6.92	

[‡] Missing values n=396 were excluded from analysis.

[¥] Missing values n=116 were excluded from analysis.

^β Missing values n=229 were excluded from analysis.

* p-values are based on Chi-square test, except for maternal age where independent sample t-test was used.

** Difference is statistically significant within p=0.05

*** Difference is statistically significant equal to or within p=0.001

Table 1b – Obstetric characteristics during the study period, before and after Oct 6th 2008

Obstetric characteristics	Category of characteristics	Precrisis (N=11,111)		Postcrisis (N=5,160)		p-value*
Mean birth weight (g) (SD)		3,693.7 (569.38)		3,665.7 (570.31)		0.003
Mean gestational length ^Φ (days) (SD)		279.54 (12.01)		279.02 (11.91)		0.011
		Births, <i>n</i>	Births, %	Births, <i>n</i>	Births, %	
Mode of delivery	Vaginal	9,279	83.51	4,344	84.18	0.278
	Caesarian section	1,832	16.49	816	15.82	
Infant's gender [€]	Male	5,763	51.88	2,630	50.97	0.281
	Female	5,346	48.12	2,530	49.03	
Apgar 5min	7-10	10,868	97.82	5,050	97.87	0.850
	<7	242	2.18	110	2.13	
Congenital malformation	No	10,716	96.44	4,964	96.22	0.440
	Yes	395	3.56	196	3.78	
Early neonatal death (<7 days)	No	11,102	99.92	5,157	99.94	0.617
	Yes	9	0.08	3	0.06	
Seasonal variation of birth weight (g) (SD)	Mar-May	3,709.21 (557.51) †		3,671.79 (576.77) ††		
	June - August	3,692.43 (577.09)		3,647.22 (591.67)		
	Sep-Nov	3,707.51 (566.44)		3,688.03 (554.59)		
	Dec - Feb	3,663.33 (575.43)		3,648.04 (566.31)		

^Φ Missing values n=8

[€] Missing values n=2

* *p*-values are based on Chi-square test, except for birth weight and gestational length where linear regression analysis, adjusted for maternal age, parity and seasonality was used. Significance level is 0.05.

† Test for homogeneity of seasonal subsets - Tukey's reveals that June-August and Dec-Feb subsets are significantly different from the other.

†† test for homogeneity of the seasonal subsets - Tukey's. - Subsets are homogenous

Table 2 - Adjusted odds ratio and 95% CI for preterm birth, low birth weight and small for gestational age during the two study periods, before and after October 6th 2008

Characteristics	Pre-crisis N=11,111		Post-crisis N=5,159		Model I*	Model II**
	Births, n	Births, %	Births, n	Births, %	OR (95% CI)	OR (95% CI)
Low birth weight (<2500 g)	274	2.47	155	3.00	1.24 (1.02 - 1.52)	1.17 (0.95 - 1.44)
Preterm birth (<37 weeks)	477	4.30	239	4.63	1.08 (0.92 - 1.26)	1.04 (0.88 - 1.22)
Small for gestational age (SGA) [∞]	151	1.36	77	1.49	1.14 (0.86 - 1.51)	1.09 (0.82 - 1.46)

*Odds ratio adjusted for maternal age (continuous variable), parity. Models involving LBW and SGA were further adjusted for seasonal variation of birth weight

** Odds ratio adjusted for seasonal variation of birth weight; employment status, relationship status, parity, residence, diabetes, hypertension, maternal age (continuous variable) and infant's gender.

[∞]SGA is inherently adjusted for infant's gender

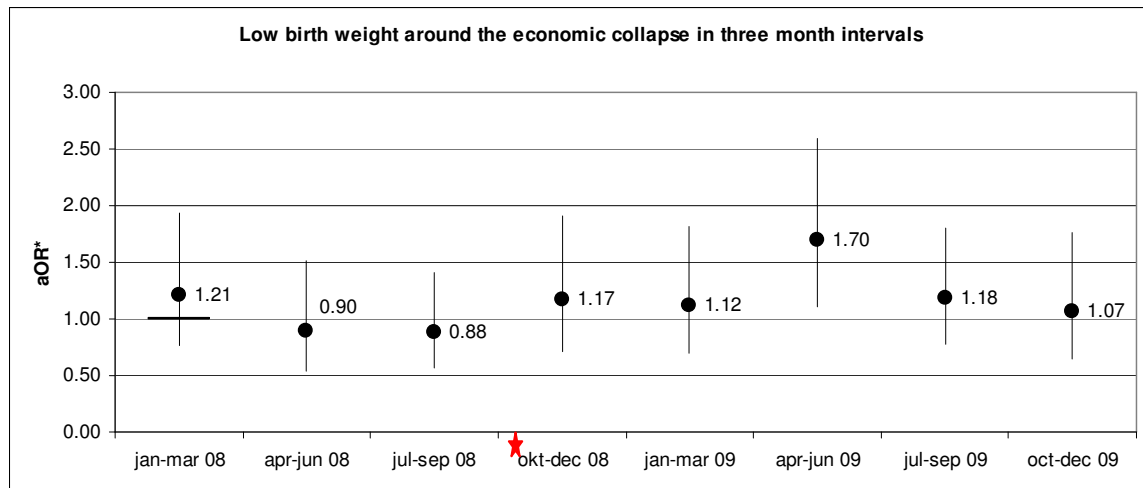
Table 3 – Adjusted odds ratio of low birth weight (<2500 g) and small-for-gestational age during the study period, before and after Oct 6th 2008, stratified by maternal characteristics

Characteristics	Category of characteristics	aOR _{LBW} * (95% CI)	aOR _{SGA} * (95% CI)
Age (year)	<25	1.85 (1.25 - 2.72)**	1.85 (1.08 - 3.19)**
	25-34	1.04 (0.78 - 1.38)	0.81 (0.54 - 1.22)
	≥35	1.21 (0.78 - 1.88)	1.36 (0.78 - 2.39)
Parity	nulliparous	1.26 (0.95 - 1.67)	1.05 (0.72 - 1.53)
	primiparous	1.08 (0.73 - 1.61)	1.11 (0.62 - 2.00)
	multiparous	1.44 (0.94 - 2.20)	1.40 (0.77 - 2.56)
Relationship status	Cohabiting with father	1.14 (0.90 - 1.45)	1.18 (0.85 - 1.64)
	Single	1.39 (0.93 - 2.08)	1.01 (0.58 - 1.76)
Place of resident	rural	1.54 (1.08 - 2.19)**	1.33 (0.82 - 2.17)
	urban	1.11 (0.86 - 1.41)	1.07 (0.76 - 1.50)
Employment status	In work	1.12 (0.88 - 1.43)	0.94 (0.67 - 1.32)
	Not working	1.59 (1.10 - 2.31)**	1.84 (1.09 - 3.10)**
Diabetes	No	1.21 (0.99 - 1.50)	1.12 (0.84 - 1.49)
	Yes	1.74 (0.71 - 4.28)	1.94 (0.42 - 9.07)
Hypertension	No	1.21 (0.95 - 1.53)	1.04 (0.74 - 1.47)
	Yes	1.24 (0.82 - 1.90)	1.25 (0.76 - 2.07)
Infants' gender	Male	1.13 (0.85 - 1.50)	
	Female	1.37 (1.03 - 1.82)**	

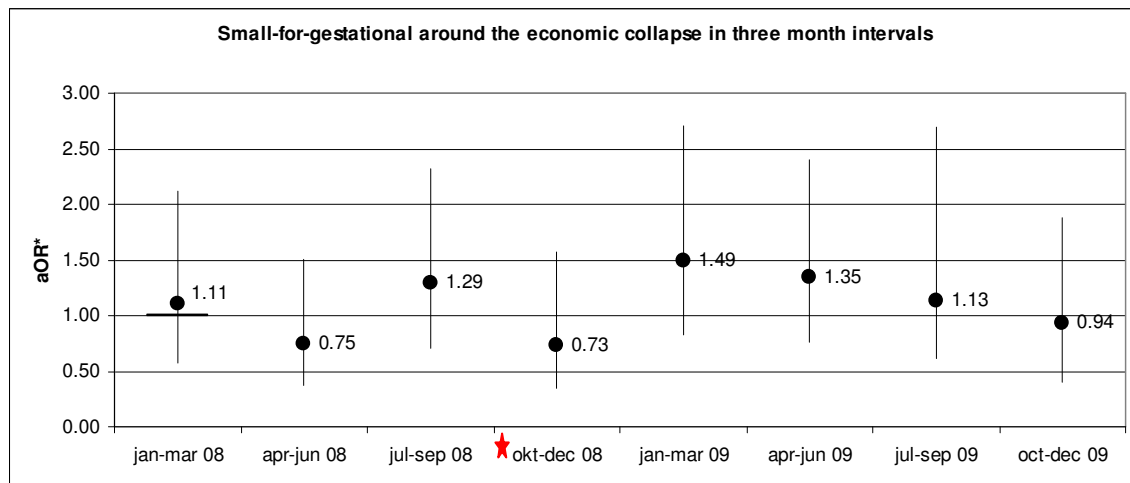
* OR adjusted for maternal age (continuous variable); parity and seasonal variation of birth weight.

** Statistically significant difference between the time periods.

(a)



(b)



(c)

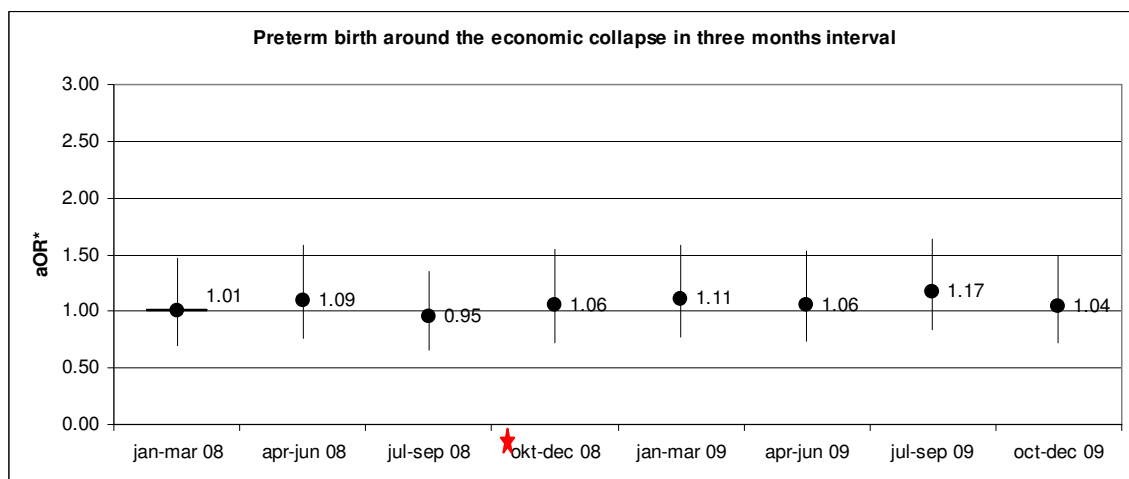


Figure 2 – Odds ratio and 95% CI for (a) low birth weight, (b) small-for-gestational age and (c) preterm birth infants in Iceland for 8 three months intervals, prior to and after the economic collapse compared with the same intervals from each of two years before.

*Odds ratio adjusted for maternal age and parity.