Stillbirth: A Selected Annotated Bibliography

Vashevnik S, Walker S, Permezel M.
Stillbirths and neonatal deaths in appropriate, small and large birthweight for gestational age fetuses.

Aims: To compare the risk of stillbirth and neonatal death in small-for-gestational-age (SGA), appropriate-for-gestational-age (AGA) and large-for-gestational-age (LGA) fetuses and neonates. Design: Retrospective analysis of 662,043 births and outcomes recorded in the Victorian Perinatal Data Collection Unit (1992-2002). Inclusion criteria: Births in Victoria in 1992-2002. Exclusion criteria: Multiple pregnancy and congenital birth defects. Main outcome measures: Births, stillbirths and neonatal deaths at each week of gestation after 23 weeks were stratified by birthweight into appropriate, small and large for gestational age. Stillbirth risk per 1000 ongoing pregnancies and neonatal death rate per 1000 live births were calculated. Results: For the AGA group, the overall stillbirth risk was 2.88 per 1000 and neonatal death rate was 1.35 per 1000. In the LGA group, these were 2.62 and 1.83 per 1000, respectively. The slight increase in neonatal death rate among LGA fetuses was confined to those delivered after 28 weeks gestation. In the SGA group, the stillbirth risk and neonatal death rate were 15.1 and 3.99 per 1000, respectively. Conclusion: The risk of stillbirth per week of gestational age and neonatal death rates do not differ significantly between AGA and LGA fetuses and neonates. The SGA fetus is at significantly greater risk of both stillbirth and neonatal death, particularly with advancing gestational age.


Heringstad B, Chang YM, Svendsen M, Gianola D.
Genetic analysis of calving difficulty in Norwegian Red cows.

The objectives of this study were to infer genetic parameters for stillbirth (SB) and calving difficulty (CD) and to evaluate phenotypic and genetic change for these traits in the Norwegian Red breed. Stillbirth is recorded as a binary trait and calving difficulty has 3 categories: 1) easy calving, 2) slight problems, and 3) difficult calving. The overall mean frequency of SB in Norwegian Red was 3% at first calving and 1.5% for second and later calvings; mean frequency of the category "difficult calving" was 2 to 3% for heifers and 1% for cows at second and later calvings. Mean stillbirth rate has remained unchanged from 1978 to 2004. The proportion of the category "difficult calving" has not changed over the years, but the "slight problems" category increased from 4 to 7% for heifers and from 2 to 3% for cows. A total of 528,475 first-calving records were analyzed.
with a Bayesian bivariate sire-maternal grandsire threshold liability model. Posterior means of direct and maternalheritabilities were 0.13 and 0.09 for CD, and 0.07 and 0.08 for SB, respectively. Strong genetic correlations were found between direct SB and direct CD (0.79), and between maternal SB and maternal CD (0.62), whereas all genetic correlations between direct and maternal effects within or between traits were close to zero. These positive correlations are favorable in the sense that selection for one of the traits would result in a favorable selection response for the second trait. No genetic correlations between direct and maternal effects imply that bulls should be evaluated both as sire of the calf (direct) and sire of the cow (maternal). No genetic change for SB was found, and a slight genetic improvement for CD was detected.


Hogberg L, Cnattingius, S.

**Influence of maternal smoking habits on the risk of subsequent stillbirth: Is there a causal relation?**


**OBJECTIVE:** Maternal smoking has previously been associated with risk of stillbirth. If women who quit smoking reduce their risk of stillbirth, the hypothesis of a causal association would be supported. **DESIGN:** Prospective cohort study. **SETTING:** Nationwide study in Sweden. **POPULATION:** All primiparous women who delivered their first and second consecutive single births between 1983 and 2001, giving a total number of 526,691 women. **METHOD:** A population-based Swedish study with data from the Medical Birth Registry, the Immigration Registry and the Education Registry. Logistic regression analyses were used to estimate odds ratios, using 95% confidence intervals. **MAIN OUTCOME MEASURE:** Stillbirth in the second pregnancy. **RESULTS:** Compared with nonsmokers in both pregnancies, women who smoked during the first pregnancy but not during the second do not have an increased risk of stillbirth (OR 1.02; 95% CI 0.79-1.30), while corresponding risk among women who smoked during both pregnancies was 1.35 (95% CI 1.15-1.58). **CONCLUSION:** The result supports that maternal smoking during pregnancy is causally associated with stillbirth risk. Smoking is a preventable cause of stillbirth, and smoking interventions is an important issue in antenatal care.

Full-text available at: [www.blackwell-synergy.com](http://www.blackwell-synergy.com) (not a U.S. Government site)


**Work-up of stillbirth: A review of the evidence.**


Despite improvements in antenatal and intrapartum care, stillbirth, defined as in utero fetal death at 20 weeks of gestation or greater, remains an important, largely unstudied, and poignant problem in obstetrics. More than 26,000 stillbirths were reported in the United States in 2001. Although several conditions have been linked to stillbirth, it is
difficult to define the precise etiology in many cases. This paper reviews known and suspected causes of stillbirth including genetic abnormalities, infection, fetal-maternal hemorrhage, and a variety of medical conditions in the mother. The proportion of stillbirths that have a diagnostic explanation is higher in centers that conduct a defined and systematic evaluation. The evidence for recommended diagnostic tests for stillbirth are discussed. The ongoing work of the National Institute of Child Health and Human Development Stillbirth Collaborative Research Network, a consortium of 5 academic centers in the United States that are studying the scope and causes of stillbirth, is presented.

Full text available at: www.sciencedirect.com (not a U.S. Government site)

Cole JB, Wiggans GR, Van Raden PM

Genetic evaluation of Stillbirth in United States holsteins using a sire-maternal grandsire threshold model.

A sire-maternal grandsire threshold model was used for genetic evaluation of stillbirth in US Holsteins. Calving ease and stillbirth records for herds reporting at least 10 dead calves were extracted from the Animal Improvement Programs Laboratory database. About half of the 14 million calving ease records in the database had a known livability score, mostly from herds processed by Dairy Records Management Systems (Raleigh, NC). Calf livability scores of 2 and 3, representing calves born dead and calves that died within 48 h of parturition, respectively, were combined into a single category. The model included effects of herd-year, year-season, parity-sex, sire, birth year group of sire, maternal grandsire (MGS), and birth year group of MGS. Herd-year, sire, and MGS were random effects. Mean predicted transmitting abilities, expressed as the expected percentage of stillbirths, were 7.9 and 8.6 for direct and maternal stillbirths, respectively. Mean reliabilities for both the direct and maternal effects were 45%. Correlations among domestic and Interbull stillbirth solutions on the underlying scale for bulls with at least 90% reliability ranged from 0.63 to 0.90 across countries for direct stillbirths and from 0.69 to 0.96 for maternal stillbirths, indicating that results were generally consistent with those from other countries. There was no evidence of a genetic trend for either trait. More complete recording of stillbirth scores would improve reliabilities and could allow for evaluations of other breeds.

Full-text available at: http://jds.fass.org/ (not a U.S. Government site)

Smith GC.

Predicting antepartum stillbirth.

Purpose of Review: Rates of stillbirth in the developed world have been static or rising in recent years. Clinical prediction of stillbirth risk may allow interventional studies. Recent Findings: The most prevalent independent risk factors are nulliparity, advanced age and obesity. These are increasingly prevalent in the developed world. Obesity is particularly
associated with stillbirth at term and after term. Pregestational diabetes is a major risk factor for stillbirth and these women are usually offered intensive surveillance during pregnancy. Despite this, a recent national study in the UK demonstrated a fourfold excess of stillbirth, with 80% unrelated to congenital abnormality. Studies of association between previous caesarean section and subsequent stillbirth risk are inconsistent, although in data sources with detailed information, the association has been confirmed. Global analyses of stillbirth risk demonstrate that 98% occur in the developing world and that many are due to potentially preventable causes. A randomized controlled trial of very simple educational interventions was associated with a 30% lower risk of stillbirth.

Summary: Relatively simple interventions may be successful in reducing the global burden of stillbirth. Further biological understanding of the causes of stillbirth is required to reduce the burden of the disease in the developed world.

Full-text available at: http://www.co-obgyn.com (not a U.S. Government site)


Litter characteristics at birth were recorded in 4 genetic types of sows with differing maternal abilities. Eighty-two litters from F(1) Duroc x Large White sows, 651 litters from Large White sows, 63 litters from Meishan sows, and 173 litters from Laconie sows were considered. Statistical models included random effects of sow, litter, or both; fixed effects of sow genetic type, parity, birth assistance, and piglet sex, as well as gestation length, farrowing duration, piglet birth weight, and litter size as linear covariates. The quadratic components of the last 2 factors were also considered. For statistical analyses, GLM were first considered, assuming a binomial distribution of stillbirth. Hierarchical models were also fitted to the data to take into account correlations among piglets from the same litter. Model selection was performed based on deviance and deviance information criterion. Finally, standard and robust generalized estimating equations (GEE) procedures were applied to quantify the importance of each effect on a piglet's probability of stillbirth. The 5 most important factors involved were, in decreasing order (contribution of each effect to variance reduction): difference between piglet birth weight and the litter mean (2.36%), individual birth weight (2.25%), piglet sex (1.01%), farrowing duration (0.99%), and sow genetic type (0.94%). Probability of stillbirth was greater for lighter piglets, for male piglets, and for piglets from small or very large litters. Probability of stillbirth increased with sow parity number and with farrowing duration. Piglets born from Meishan sows had a lower risk of stillbirth (P < 0.0001) and were little affected by the sources of variation mentioned above compared with the 3 other sow genetic types. Standard and robust GEE approaches gave similar results despite some disequilibrium in the data set structure highlighted with the robust GEE approach.

Full-text available at: http://jas.fass.org/ (not a U.S. Government site)

Saflund K, Wredling R.
Differences within couples' experience of their hospital care and well-being three months after experiencing a stillbirth.

Background: The present study aimed to investigate possible differences, within the couple, in their encounter with their stillborn child and the assistance of caregivers during the event and to evaluate the parents' psychological well-being three months after the stillbirth. Methods: Twenty-two couples, who experienced a stillbirth, participated in the study. A study-specific questionnaire and a previously evaluated well-being questionnaire were used to assess the parents' psychological condition. Chi-square analysis, Wilcoxon's signed rank test, Student's paired t-test, and Spearman's rank correlation coefficient were used to detect differences within the couples. Results: The parents had feelings of fear when they conceptualized the stillborn child, but with support from staff all but one couple held their child. The fathers had the same strong feelings of warmth, pride, tenderness, and grief as the mothers when they held the child. Most parents reported that the staff had treated them with understanding during the delivery. Three months after the event the mothers scored significantly higher on Negative Well-being, lower on Positive Well-being, and lower on General Well-being than the fathers. A majority of the mothers, but no fathers, were on sick leave three months after the event. Conclusions: Our study suggests that mothers and fathers need to be emotionally supported in the encounter with their stillborn child. The mothers' scoring of lower well-being may be due to a stronger antenatal attachment to the child. This should, however, be a subject of further studies.


Smith GC, Shah I, White IR, Pell JP, Dobbie R.

Women with a previous stillbirth are known to be at increased risk of stillbirth in subsequent pregnancies. However, few studies have addressed the association between other complications of pregnancy and the future risk of stillbirth. Using linkage of national pregnancy and perinatal death registries, the authors performed a retrospective cohort study of 133,163 women having a second birth in Scotland between 1992 and 2001 whose first infant was liveborn. The risk of unexplained stillbirth was increased among women with a previous preterm birth (adjusted hazard ratio (HR) = 2.04, 95% confidence interval (CI): 1.34, 3.11), previous delivery of a small for gestational age (SGA) infant (HR = 2.14, 95% CI: 1.59, 2.87), and previous preeclampsia (HR = 1.68, 95% CI: 1.07, 2.62). The associations were similar after adjustment for maternal age, height, marital and smoking status, and interpregnancy interval. There was a statistically significant positive interaction between previous delivery of a SGA infant and previous preeclampsia (p = 0.01): Women with this combination in their first pregnancy had an approximately fivefold risk of unexplained stillbirth in the second pregnancy (HR = 4.95, 95% CI: 2.63, 9.32). Associations were stronger with SGA unexplained stillbirths. The
authors conclude that complicated first births of liveborn infants are associated with an increased risk of unexplained stillbirth in the next pregnancy.


Fellman J, Eriksson AW.
Stillbirths in multiple births: test of independence.

The stillbirth rate in twins is a more sensitive indicator of environmental hazards than the stillbirth rate in singletons. Medical care or other socioeconomic factors may be more influential for perinatal survival in twin than in single deliveries. Studies have indicated that stillbirths among children in a set of multiple maternities are not independent. Models were considered assuming independent outcomes within a set of multiple maternities. Analyses of the stillbirth rates confirm that the risk of stillbirth among males is almost constantly higher than among females. Any model introduced should assume different stillbirth rates for males and females. The models were tested with both maximum likelihood and minimum chi2 methods. Data was analyzed from Sweden, the Aland Islands, Saxony, England and Wales, and significant discrepancies obtained from the independence models. The same-sexed twin data contain both monozygotic and dizygotic twin sets with apparently different stillbirth rates. Consequently, for same-sexed twins the proposed model could be considered too simple. After improvement by splitting the same-sexed data into monozygotic and dizygotic twin sets, the dependence still remains. The proportion of both same-sexed and opposite-sexed twin pairs that contain two stillborn is greater than what the stillbirth rates and the independence should indicate. Consequently, stillbirth rate estimates based on the relative frequency of twin sets with two stillborn children have a positive bias. When the stillbirth rate decreases, the number of sets with two stillborn children decreases more slowly than would be indicated by independence.

Full-text available at:

Salihu HM, Sharma PP, Peters S.
Twinning and risk of stillbirth subtypes in pediatric mothers.

We sought to estimate levels of risk for stillbirth subtypes associated with twin gestations among pediatric mothers (10-14 years). Analysis was on twin pregnancies covering the period 1989 to 2000 in the United States. We classified stillbirth as term, preterm, small-for-gestational-age (SGA) or preterm-SGA. We then assessed the risks of these stillbirth subtypes in pediatric mothers using two comparison groups consisting of women aged 15 to 19 years old (adolescent mothers) and 20 to 24 years old (mature mothers). Adjusted risk estimates were by means of hazard ratios generated from a Cox proportional hazards regression model. We adjusted for dependence of observations within twin clusters using
the robust sandwich estimator. The rate of stillbirth was highest among pediatric mothers (56/1000), followed by adolescent gravidas (29/1000) and lowest in mature mothers (20/1000; p for trend < .01). Overall, preterm stillbirth was the most frequent stillbirth phenotype while term stillbirth was the least frequent. Not a single case of term stillbirth was recorded in pediatric mothers. Among pediatric gravidas, the risk for preterm stillbirth was more than tripled (adjusted hazard ratio [AHR] = 3.4; 95% confidence interval [CI] = 2.5-4.6), and that of preterm-SGA stillbirth more than doubled (AHR = 2.6; 95% CI = 1.8-3.7) that of mature mothers respectively. The 30% risk elevation for SGA stillbirth among pediatric mothers was not found to be statistically significant (AHR = 1.1; 95% CI = 0.3-4.3). Pediatric motherhood is a risk factor for stillbirth in twin gestation, especially, preterm and preterm-SGA stillbirth phenotypes. Prevention of stillbirth among this category of mothers should target the period preceding full term.


Objective: In England an estimated 50,000 inductions of labour at or beyond 41 weeks' gestation are conducted each year. However, the published evidence on the effect of parity on stillbirth in prolonged pregnancy is limited, and has produced conflicting data. The aim of this study is to evaluate the influence of parity on fetal mortality in prolonged pregnancies. Study Design: Retrospective analysis of 145,695 singleton births with known parity and no malformation noted at birth to residents in the former North-East Thames Region, UK. The parity and gestation specific stillbirth risks and relative risks per 1000 ongoing pregnancies were calculated in relation to parity between 37 and 45 weeks. Results: Before 41 weeks the stillbirth risk rose gradually but did not differ by parity. By 41 weeks there was a substantial increase in the stillbirth risk in nulliparous women but not in parous women. The pattern of rise is such that the stillbirth risk is 2.9 times higher (95% CI 1.06-8.19) in nulliparous women at >42 weeks' gestation. Conclusion: Being parous appears to have a protective effect on fetal mortality in prolonged pregnancy. These findings question the need for routine induction of labour at 41 weeks in parous women.

Full-text: http://www.sciencedirect.com (not a U.S. Government site)


Objective: This study aimed to determine whether neuroticism and educational level predict posttraumatic stress disorder (PTSD) in women following an unsuccessful
pregnancy. Method: Via advertisements, pregnant women with a gestational period shorter than 12 weeks were asked to participate in a study regarding their perception of pregnancy. After they had agreed, they were sent questionnaires, including a scale for neuroticism and their highest attained educational level. Every other month during the pregnancy and 1 month after the expected date of birth, they were sent brief questionnaires about the pregnancy. Participants for whom the pregnancy had ended unsuccessfully were contacted by phone and asked to participate in a follow-up study with a PTSD scale. Results: Of the 1339 women studied, 126 (9%) experienced an unsuccessful pregnancy; 8 of these dropped out of the study (response rate, 94%); 1 had not indicated her educational level. The remaining 117 women filled out the PTSD scale after about 1 month. Thirty-one women (26%) met the DSM-IV criteria for PTSD and 86 women did not. Logistic regression analysis revealed that PTSD was significantly associated with higher neuroticism, lower educational level and longer duration of gestation. Conclusion: For patients with a high educational level and low neuroticism score, the risk of developing PTSD was negligible, while for those with a low educational level and a high score for neuroticism, the estimated risk was about 70%. Care and guidance should focus primarily on the latter group.

Reddy UM, Ko CW, Willinger M. 
Maternal age and the risk of stillbirth throughout pregnancy in the United States. 

Objective: The objective of the study was to examine the relationship of maternal age with stillbirth risk throughout gestation. Study Design: A total of 5,458,735 singleton gestations without reported congenital anomalies from the 2001 to 2002 National Center for Health Statistics perinatal mortality and natality files were analyzed. Hazard rates (risk) of stillbirth (fetal death 20 weeks or longer) were calculated for each week of gestation. Results: The risk of stillbirth at 37 to 41 weeks for women 35 to 39 years old was 1 in 382 ongoing pregnancies and for women 40 years old or older, 1 in 267 ongoing pregnancies. Compared with women younger than 35 years old, the relative risk of stillbirth was 1.32 (95% confidence interval 1.22, 1.43) for women 35 to 39 years old and 1.88 (95% confidence interval 1.64, 2.16) for women 40 years old or older at 37 to 41 weeks. This effect of maternal age persisted despite accounting for medical disease, parity, and race/ethnicity. Conclusion: Women who are of advanced maternal age are at higher risk of stillbirth throughout gestation; the peak risk period is 37 to 41 weeks.

Full-text: http://journals.elsevierhealth.com/periodicals/ymob (not a U.S. Government site)

Mohsin M, Bauman AE, Jalaludin B. 
Influence of antenatal and maternal factors on stillbirths and neonatal deaths in New South Wales, Australia. 

This study identified the influences of maternal socio-demographic and antenatal factors on stillbirths and neonatal deaths in New South Wales, Australia. Bivariate and
multivariate analyses were used to explore the association of selected antenatal and maternal characteristics with stillbirths and neonatal deaths. The findings of this study showed that stillbirths and neonatal deaths significantly varied by infant sex, maternal age, Aboriginality, maternal country of birth, socioeconomic status, parity, maternal smoking behaviour during pregnancy, maternal diabetes mellitus, maternal hypertension, antenatal care, plurality of birth, low birth weight, place of birth, delivery type, maternal deaths and small gestational age. First-born infants, twins and infants born to teenage mothers, Aboriginal mothers, those who smoked during the pregnancy and those of lower socioeconomic status were at increased risk of stillbirths and neonatal deaths. The most common causes of stillbirths were conditions originating in the perinatal period: intrauterine hypoxia and asphyxia. Congenital malformations, including deformities and chromosomal abnormalities, and disorders related to slow fetal growth, short gestation and low birth weight were the most common causes of neonatal deaths. The findings indicate that very low birth weight (less than 2000 g) contributed 75·6% of the population-attributable risks to stillbirths and 59·4% to neonatal deaths. Low gestational age (less than 32 weeks) accounted for 77·7% of stillbirths and 87·9% of neonatal deaths. The findings of this study suggest that in order to reduce stillbirths and neonatal deaths, it is essential to include strategies to predict and prevent prematurity and low birth weight, and that there is a need to focus on anti-smoking campaigns during pregnancy, optimizing antenatal care and other healthcare programmes targeted at the socially disadvantaged populations identified in this study.

Full-text available at: http://journals.cambridge.org (not a U.S. Government site)

McClure EM, Nalubamba-Phiri M, Goldenberg RL
Stillbirth in developing countries.

Objective: To conduct a systematic review of the literature on stillbirths in developing countries. Method: Review of the English literature for all articles related to stillbirth in developing countries published from 1975 to 2005. Results: Because almost half of the deliveries in developing countries occur at home, under-reporting of stillbirths is a huge problem, and reliable data about rates and causes are difficult to obtain. Hospital stillbirth data are often subject to substantial bias and the ability to generalize from these data is unknown. Nevertheless, at least 4 million stillbirths occur yearly, the vast majority in developing countries, with rates in many developing countries ten-fold higher than elsewhere. Prolonged and obstructed labor, preeclampsia and various infections, all without adequate treatment, account for the majority of stillbirths. Conclusion: Despite the large number of stillbirths worldwide, the topic of stillbirths in developing countries has received very little research, programmatic or policy attention. Better access to appropriate obstetric care, especially during labor, should reduce developing country stillbirth rates dramatically.

Robson S, Thompson J, Ellwood D.

**Obstetric management of the next pregnancy after an unexplained stillbirth: an anonymous postal survey of Australian obstetricians.**


Background: Women who have an unexplained stillbirth are more likely to be delivered early, by induced labour or Caesarean section, in their next pregnancy. It is unclear whether these birth outcomes result from characteristics of the next pregnancy, or represent management strategies of obstetricians. Aim: To investigate obstetricians' management strategies in the next pregnancy after an unexplained stillbirth. Methods: Anonymous postal survey of Australian obstetricians. Respondents were given a clinical scenario regarding a previous unexplained stillbirth and were asked about management. Results: The response rate was 69%. Tests of 'fetal well-being' were undertaken by the majority of respondents. Additional third trimester ultrasound surveillance was recommended by 87% of respondents, regular cardiotograph monitoring by 72% and formal fetal movement charting by 39%. Elective induction of labour (in the absence of any other obstetric indication) was recommended by 93% of respondents, and elective Caesarean delivery by 35%. Conclusions: The tendency for subsequent pregnancies after an unexplained stillbirth to be delivered earlier, and more often by Caesarean section, may be due in part to altered management strategies, not solely as a result of complications of the pregnancy itself.


Dodds L, King WD, Fell DB, Armson BA, Allen A, Nimrod C.

**Stillbirth risk factors according to timing of exposure.**


Purpose: The purpose of the present study is to identify risk factors for stillbirth and explore hypotheses about the cause of stillbirth based on the time in gestation when exposures occur. Methods: Relationships between lifestyle factors, pregnancy conditions, medication use, and occupation on risk for stillbirth were examined within a population-based case-control study. Women who had a stillbirth and a random sample of women who had a live birth between 1999 and 2001 were identified through perinatal databases in Nova Scotia and Eastern Ontario, Canada. Exposure data were collected for each month of pregnancy and analyzed within trimesters. Case-control data were converted to case-cohort data, and hazard ratios (HRs) and 95% confidence intervals (CIs) were determined from Cox proportional hazards models. Results: This study included 105 stillbirth cases and 389 live-birth controls. Fertility treatment in the present pregnancy was associated with increased risk for stillbirth (adjusted HR, 4.0; 95% CI, 1.4-11.6). Smoking during the first trimester also was associated with increased risk for stillbirth (adjusted HR, 2.4; 95% CI, 1.2-4.9). Other risk factors included antiemetic use during the first trimester, second-trimester antibiotic use, low family income, and age older than 35 years. Conclusions: Risk factors identified in this study concur with findings of previous studies and support the importance of early pregnancy exposures on stillbirth risk.
Ahmed S, Koenig MA, Stephenson R.
Effects of domestic violence on perinatal and early-childhood mortality: Evidence from north India.

Objective: We examined the effect of physical violence during pregnancy on perinatal and early-childhood mortality. Methods: We estimated the prevalence of domestic violence during pregnancy among a population-based sample of 2199 women in Uttar Pradesh, India. We used a survival regression model to examine the risks for perinatal, neonatal, postneonatal, and early-childhood (aged 1-3 years) mortality by mother's exposure to domestic violence, after we controlled for other sociodemographic and maternal health behavior risk factors. Results: Eighteen percent of the women in our study experienced domestic violence during their last pregnancy. After we adjusted for other risk factors, births among mothers who had experienced domestic violence had risks for perinatal and neonatal mortality that were 2.59 (95% confidence interval [CI]=1.35, 4.95) and 2.37 (95% CI=1.21, 4.62) times higher, respectively, than births among mothers who had not experienced violence. We found no significant associations between domestic violence and either postneonatal or early-childhood mortality. Conclusions: Domestic violence is a significant risk factor for perinatal and neonatal mortality.

Full-text available at: http://www.ajph.org (not a U.S. Government site)

Richter R, Bergmann RL, Dudenhausen JW.
Previous caesarean or vaginal delivery: Which mode is a greater risk of perinatal death at the second delivery?

Objective: To compare the risk of perinatal death after previous caesarean versus previous vaginal delivery, and pre-labour repeat caesarean versus trial of labour after previous caesarean. Study Design: Using the data of the Berlin Perinatal Registry from 1993 to 1999, 7556 second parous women with a previous caesarean delivery were compared with 55142 second parous women with a previous vaginal delivery, and those 1435 women with pre-labour repeat caesarean were compared with 6121 women with a trial of labour after previous caesarean delivery. The rates of perinatal death, stillbirth and intrapartum/neonatal death were analysed using multivariable logistic regression to adjust for confounding variables and obstetric history. Results: A previous caesarean delivery was associated with a 40% excess risk of perinatal death and a 52% excess risk of stillbirth (p<0.05); the risk of intrapartum/neonatal death was not significantly increased. There were no significantly higher rates of intrapartum/neonatal death and of stillbirth in women trying a vaginal birth versus pre-labour repeat caesarean. But in most cases of antepartum death, labour was induced for that reason. Conclusion: Consulting women about caesarean delivery for maternal request, the increased risk of perinatal death in
further pregnancies should be discussed. After a previous caesarean delivery, a careful screening for several risk factors is necessary before recommending a trial of labour.


Adewuya AO, Ola BA, Aloba OO, Dada AO, Fasoto OO. Prevalence and correlates of depression in late pregnancy among Nigerian women. Depress Anxiety. 2006 Jul 14; [E-pub ahead of print]

The objectives of this study were to estimate the prevalence of depressive disorder in late pregnancy in a group of Nigerian women and to examine the associated factors. One hundred and eighty women in late pregnancy completed a questionnaire on sociodemographic and obstetrical details. They also completed the Edinburgh Postnatal Depression Scale (EPDS). A proportion of them were then assessed for the DSM-IV diagnosis of depressive disorder. Fifteen (8.3%) women met the current (2 weeks) DSM-IV diagnosis of depressive disorder. The factors independently associated with depression included being single [odds ratio (OR)=16.67, 95% confidence interval (CI)=3.17-87.76], divorced/separated (OR=11.11, 95% CI=1.55-19.65), polygamous (OR=3.92, 95% CI=0.94-16.33), and having a previous history of stillbirth (OR=8.00, 95% CI=1.70-37.57) and perceived lack of social support (OR=6.08, 95% CI=1.42-26.04). Depression is common in late pregnancy among Nigerian women, with the significant correlates including mainly social and family factors. Such factors should be considered when planning health care services or formulating a predictive model. Interventions aimed at reducing the occurrence of antenatal depression need further research.


Background: The objective of this study was to determine the institutional pregnancy loss rate following second-trimester genetic amniocentesis and to ascertain whether factors exist which would identify pregnancies at increased risk of having a procedure-related fetal loss. Setting: University Teaching Hospital Methods: Details of the procedure and pregnancy outcome of all patients who had amniocentesis planned or performed between 15-22 gestational weeks between January 1997 and June 2004 were extracted from our clinical audit database. The procedure-related fetal loss rate, defined as all unintended abortions, stillbirths and neonatal deaths without major fetal abnormalities or obvious obstetric causes, was determined and compared to a presumed background fetal loss rate of 0.8% based on a cohort of women who did not undergo the procedure. Results: A total of 3468 consecutive amniocenteses were performed in 3440 patients with 3498 fetuses. The mean gestational age at amniocentesis was 17.6 +/- 1.2 weeks. The majority (98.6%) required only one puncture and a transplacental procedure was required in 2.7% cases. A
total of 3465 chromosomal studies were performed. Sixty six cases (1.9%) of major chromosomal abnormalities were detected. Pregnancy outcome was ascertained in all except 26 singleton pregnancies (0.74%). There were 3285 (93.9%) livebirths, 103 (2.9%) termination of pregnancies (TOP), 6 (0.17%) fetal demises before the procedure, and 20 (0.61%) unintended fetal losses due to significant fetal abnormalities or obstetric complications. The remaining 58 fetal losses (1.66%) were classified as potentially procedure-related, which could be either background fetal losses or procedure-related. The procedure-related fetal loss rate after correcting for the background loss rate was 0.86%. Potentially procedure-related fetal losses were found to be significantly associated with a procedure at 18 weeks or beyond (odds ratio OR = 1.97), a procedure performed for abnormal second-trimester biochemical screening test (OR = 3.08), a bloody tap (OR = 6.48), and a female fetus (OR = 2.39); but not to the number of punctures (p = 0.66) nor transplacental amniocentesis (p = 0.104). Conclusions: Mid-trimester amniocentesis is associated with a small but significant risk of fetal loss of 0.86%.


Nohr EA, Frydenberg M, Henriksen TB, Olsen J.

Does low participation in cohort studies induce bias?

Background: Participation rates in large cohort studies have decreased during the last 2 decades. The consequences of this trend for relative risk estimation are unknown. Methods: The impact of a low participation rate (30%) on the Danish National Birth Cohort was examined among 49,751 women from the source population, including 15,373 participants in the cohort study. On the basis of independent data collection, we estimated odds ratios (ORs) in the source population and among participants for 3 exposure-risk associations: (a) in vitro fertilization and preterm birth, (b) smoking during pregnancy and birth of a small-for-gestational-age infant, and (c) prepregnancy body mass index and antepartum stillbirth. The effect of nonparticipation was described by a relative odds ratio (ROR), calculated as the OR (participants)/OR(source population). Two methods for calculation of confidence intervals for the relative odds ratio also were assessed. Results: The effect of nonparticipation on the selected ORs was small. The relative ORs were close to one and the bias was never larger than 16%, although some of the confidence intervals were wide. The 2 methods for calculation of confidence intervals for the relative odds ratio also were assessed. Results: The effect of nonparticipation on the selected ORs was small. The relative ORs were close to one and the bias was never larger than 16%, although some of the confidence intervals were wide. The 2 methods for calculation of confidence intervals gave very similar results and a small simulation study showed that the coverage probabilities were close to the 95% nominal level. Conclusion: For the 3 chosen associations, the ORs were not biased by nonparticipation. The results are reassuring for studies based on the Danish cohort and similar cohorts of pregnant women. The methodology used to compute confidence intervals for the relative odds ratios performed well in the scenarios considered.

Full-text available at: http://www.epidem.com (not a U.S. Government site)

Banajeh SM, Al-Rabee AM, Al-Arashi IH.
Burden of perinatal conditions in Yemen: A 12-year hospital-based study.

We conducted a 12-year retrospective analysis of perinatal characteristics at Al-Sabeen Hospital, Sana'a. There were 62168 births, 2936 stillbirths and 5434 perinatal deaths. There were 14 576 (24.6%) preterm low-birth-weight (LBW) babies. Early neonatal death (ENND) rate was 42.2/1000 live births. Of the 10 546 neonates admitted to the special baby care unit (SBCU), 40.1% were preterm LBW and 2147 (20.4%) died (80.6% were preterm LBW). The last 4 years showed a 17.2% increase in stillbirths and a 40.5% reduction in ENND compared with the first 4 years. In the SBCU, reduction in ENND was > 70%. Respiratory distress accounted for 63.8% of deaths in the SBCU and birth asphyxia 15.0%. Our results reflect the poor antenatal and delivery care services in Yemen.

Lavezzi AM, Ottaviani G, Mauri M, Matturri L.
Alterations of biological features of the cerebellum in sudden perinatal and infant death.

This article intends to show how the cerebellum, a structure ordinarily not considered in mediating breathing or cardiovascular control, may play a critical role in compensatory responses particularly to hypoxic insults occurring pre and/or postnatally and thus may be involved in the sudden unexplained perinatal and infant death. Besides the ontogenesis of the cerebellar cortex in man, we reported alterations of biopathological features (neuronal immaturity, altered apoptotic programs, negative expression of somatostatin and EN2 gene, intense c-fos expression positivity, astrogliosis) in the cortex and in the dentate nucleus of the 63% of sudden deaths, and only in 10% of the controls. The correlation of these results with the mother's smoking habit was highly significant. Therefore, we support the hypothesis, already expressed in previous studies on brainstem, of a close relation between maternal cigarette smoking and a wide range of morpho-physiological defects of the brain, leading to unexplained sudden death in stillbirths, newborns, and Sudden Infant Death Syndrome (SIDS) victims.

Full-text available at: http://www.ingentaconnect.com (not a U.S. Government site)

Haldre K, Rahu K, Karro H, Rahu M.
Is a poor pregnancy outcome related to young maternal age? A study of teenagers in Estonia during the period of major socio-economic changes (from 1992 to 2002).

Objective: To assess the risk of low birth weight, preterm birth, stillbirth, neonatal and postneonatal death among primiparous teenagers having singleton births, compared to a similar group of women aged 20-24 years in Estonia during the period of major socio-economic changes. Study Design: Registry study using the data from the Estonian Medical Birth Registry (EMBR) for years 1992-2002; EMBR data were linked with infant deaths in the Estonian Mortality Database. Study population included 51,890
women aged 13-24 years, arranged into three groups: \( \leq 17 \), 18-19, and 20-24. Crude odds ratios (OR), adjusted ORs and their 95% confidence intervals (CI) for the different outcomes were estimated using multiple logistic regression analysis. Results: Compared with women aged 20-24 years, the risk of low birth weight and preterm birth was higher among teenagers. The risk of low birth weight and preterm birth within the study group as a whole did not change during the study period. Increased risks in neonatal and postneonatal death among younger teenagers of an age of 17 years and less seem to be a result of prematurity. Conclusions: Despite major socio-economic changes resulting in improvements in obstetric care and growth in incomes, teenagers remained a higher risk group.


Maternal-Fetal Medicine Committee; Clinical Practice Obstetrics Committee; Leduc L, Farine D, Armson BA, Brunner M, Crane J, Delisle MF, Gagnon R, Keenan-Lindsay L, Morin V, Mundle RW, Scheider C, Van Aerde J.

**Stillbirth and bereavement: Guidelines for stillbirth investigation.**

Objectives: To provide an investigation protocol to help health care providers determine the cause of a fetal death. Options: Consideration has been given to protocols for the investigation of fetal death that are currently available in Canada and in other countries. Outcomes: Identification of possible causes of stillbirth and their relationship to future pregnancies. Evidence: Articles related to the etiology of fetal death were identified in a search of MEDLINE (January 1993 to December 2004), the Cochrane Library, and investigation protocols from the American College of Obstetricians and Gynecologists, the Alberta Medical Association Committee on Reproductive Care, and the Centers for Disease Control and Prevention National Center for Health Statistics. Benefits: To provide better advice for women regarding possible causes of fetal death and implications for future pregnancies. Recommendation: A protocol should be used to investigate the possible cause of a fetal death. (II-B) Validation: The evidence obtained was reviewed and evaluated by the Maternal-Fetal Medicine Committee and the Clinical Practice Obstetrics Committee of the Society of Obstetricians and Gynaecologists of Canada. The level of evidence and quality of there commendation made was described using the Evaluation of Evidence criteria of the Canadian Task Force on the Periodic Health Examination.

Bech BH, Autrup H, Nohr EA, Henriksen TB, Olsen J.

**Stillbirth and slow metabolizers of caffeine: Comparison by genotypes.**
Int J Epidemiol. 2006 Jun 16; [E-pub ahead of print]

Background: Cytochrome P4501A2 (CYP1A2) and N-acetyltransferase 2 (NAT2) are key enzymes in the metabolism of caffeine. The polymorphism of these genes facilitates the detection of fast and slow metabolizers, and if caffeine is causally related to stillbirth, we expect slow metabolizers to have a higher risk of stillbirth at any given intake of caffeine. Glutatione S-transferase alpha1 (GSTA1) may also be active in the metabolism
of caffeine as it conjugates glutathione to aromatic amines. Our study, therefore, included analyses of the association between GSTA1 and stillbirth. Methods: A nested case non-case study among women who participated in the Danish National Birth Cohort: 142 cases of singleton stillbirths and 157 controls of singleton live births. Results: Slow oxidizer status (CYP1A2), slow acetylator status (NAT2), and low activity of GSTA1 were not individually associated with the risk of stillbirth [odds ratio (OR) = 1.06, 95% confidence interval (95% CI) 0.67-1.67, OR = 0.95, 95% CI 0.60-1.51, and OR = 1.42, 95% CI 0.88-2.28, respectively]. We did, however, observe that subjects with a combination of slow CYP1A2, slow NAT2, and low GSTA1 genes had almost a 2-fold risk of stillbirth compared with subjects with other combinations of genotypes. Conclusions: We found no link between any single genotype and the risk of stillbirth. An association between a combination of genotypes and stillbirth was discovered. Caffeine may be causally related to stillbirth, but larger studies using Mendelian randomization are needed to verify this.


Objective: The purpose of this study was to examine temporal changes in stillbirth, neonatal and infant mortality rates among triplet births in the US, and to assess the contributions of triplet delivery at <34 weeks to these changes. Study Design: Data on triplet live births, and fetal and infant deaths (1990-2002) delivered at >/=22 weeks and fetuses weighing >/=500 g (n = 66,986) were derived from the US linked birth/infant death data files. Relative risk (RR), quantifying changes in triplet stillbirth, neonatal (death within the first 28 days) and infant mortality (death within the first year) rates between 1990 and 1991 and 2001 and 2002, were derived. Temporal changes in triplet births at <34 weeks, and changes in stillbirth, and neonatal and infant mortality rates were examined through logistic regression models before and after adjusting for confounders. Results: Triplet births at <34 weeks increased by 25% between 1990 and 1991 (48.7%) and 2001 and 2002 (60.9%). Stillbirth, neonatal and infant mortality rates declined by 52% (RR 0.48, 95% confidence interval [CI] 0.36-0.63), 32% (RR 0.68, 95% CI 0.58-0.80), and 38% (RR 0.62, 95% CI 0.53-0.71), respectively, between 1990 and 1991 and 2001 and 2002. The increase in triplet births at <34 weeks was not associated with the stillbirth decline, but was associated with an excess 14% and 12% increase in neonatal and infant deaths, respectively. Conclusion: Our findings suggest that the increase in triplet births at <34 weeks’ gestation is not associated with changes in triplet stillbirths, but is associated with increases in triplet neonatal and infant mortality.


Bretveld RW, Thomas CM, Scheepers PT, Zielhuis GA, Roeleveld N.
Pesticide exposure: The hormonal function of the female reproductive system disrupted?

Some pesticides may interfere with the female hormonal function, which may lead to negative effects on the reproductive system through disruption of the hormonal balance necessary for proper functioning. Previous studies primarily focused on interference with the estrogen and/or androgen receptor, but the hormonal function may be disrupted in many more ways through pesticide exposure. The aim of this review is to give an overview of the various ways in which pesticides may disrupt the hormonal function of the female reproductive system and in particular the ovarian cycle. Disruption can occur in all stages of hormonal regulation: 1. hormone synthesis; 2. hormone release and storage; 3. hormone transport and clearance; 4. hormone receptor recognition and binding; 5. hormone postreceptor activation; 6. the thyroid function; and 7. the central nervous system. These mechanisms are described for effects of pesticide exposure in vitro and on experimental animals in vivo. For the latter, potential effects of endocrine disrupting pesticides on the female reproductive system, i.e. modulation of hormone concentrations, ovarian cycle irregularities, and impaired fertility, are also reviewed. In epidemiological studies, exposure to pesticides has been associated with menstrual cycle disturbances, reduced fertility, prolonged time-to-pregnancy, spontaneous abortion, stillbirths, and developmental defects, which may or may not be due to disruption of the female hormonal function. Because pesticides comprise a large number of distinct substances with dissimilar structures and diverse toxicity, it is most likely that several of the above-mentioned mechanisms are involved in the pathophysiological pathways explaining the role of pesticide exposure in ovarian cycle disturbances, ultimately leading to fertility problems and other reproductive effects. In future research, information on the ways in which pesticides may disrupt the hormonal function as described in this review, can be used to generate specific hypotheses for studies on the effects of pesticides on the ovarian cycle, both in toxicological and epidemiological settings.

Full-text downloading at: http://www.rbej.com/content/4/1/30 (not a U.S. Government site)

Stanton C, Lawn JE, Rahman H, Wilczynska-Ketende K, Hill K.
Stillbirth rates: Delivering estimates in 190 countries.

Background: While information about 4 million neonatal deaths worldwide is limited, even less information is available for stillbirths (babies born dead in the last 12 weeks of pregnancy) and there are no published, systematic global estimates. We sought to identify available data and use these to estimate the rates and numbers of stillbirths for 190 countries for the year 2000, and provide uncertainty estimates. Methods: We assessed three sources of stillbirth data according to specified inclusion criteria: vital registration; demographic and health surveys (DHS), based on a new analysis of contraceptive calendar data; and study reports that include published studies identified through systematic literature searches of more than 30,000 abstracts and unpublished studies. A
random effects regression model was developed to predict national stillbirth rates and associated uncertainty intervals. Findings: Data from 44 countries with vital registration (71,442 stillbirths), 30 DHS surveys from 16 countries (2989 stillbirths), and 249 study populations from 103 countries (93,023 stillbirths) met the inclusion criteria. Model-based estimates were used for 128 countries. For 62 countries, the observed values were adjusted by a correction factor derived from the model. The resultant stillbirth rates ranged from five per 1000 in rich countries to 32 per 1000 in south Asia and sub-Saharan Africa. The estimated number of global stillbirths is 3.2 million (uncertainty range 2.5-4.1 million). In light of the data limitations and the conservative approach taken, the real number might be higher than this. Interpretation: The numbers of stillbirths are high and there is a dearth of usable data in countries and regions in which most stillbirths occur, with under-reporting being a major challenge. Although our estimates are probably underestimates, they represent a rigorous attempt to measure the numbers of babies dying during the last trimester of pregnancy. Improving stillbirth data is the first step towards making stillbirths count in public-health action.

Full-text available at: http://www.lancet.com (not a U.S. Government site)

Bahtiyar MO, Julien S, Robinson JN, Lumey L, Zybert P, Copel JA, Lockwood CJ, Norwitz ER.

Am J Obstet Gynecol. 2006 May 2; [E-pub ahead of print]

Objective: An association between cesarean delivery and an increased risk of stillbirth in a subsequent pregnancy has been reported in the United Kingdom. This study investigated the association between prior cesarean delivery and unexplained intrauterine fetal demise at term in the United States. Study Design: We conducted a cross-sectional study using the U.S. perinatal mortality data (1995 to 1997). Women aged 15 to 44 years with singleton term (37 weeks or longer) pregnancies were included in the analysis. Study groups were defined as pregnant women with a prior cesarean delivery (prior cesarean delivery) and women with no prior cesarean delivery (no cesarean delivery). Adjustments were made for maternal age, race, underlying medical conditions, and fetal congenital abnormalities. The Cochran-Mantel-Haenszel method was used for relative risk estimation at the 95% confidence interval calculation. Results: A total of 11,061,599 deliveries of singleton pregnancies were recorded in the United States from January 1, 1995, to December 31, 1997. The cesarean delivery rate was 19.6%. The crude term intrauterine fetal demise rate was 1.5 per 1000 births for no cesarean delivery and 1.3 per 1000 births for prior cesarean delivery. After correction for parity greater than 1, congenital anomalies, and underlying maternal medical conditions, term intrauterine fetal demise rates were 0.6 and 0.4 per 1000 births for no cesarean delivery and prior cesarean delivery, respectively. Restriction of the analysis to women with only 1 prior delivery resulted in term intrauterine fetal demise rates of 0.8 and 0.7 per 1000 births for no cesarean delivery and prior cesarean delivery, respectively (relative risk 0.90; 95% confidence interval 0.76-1.06). Conclusion: A prior cesarean delivery is not associated with an increased risk of stillbirth in a subsequent pregnancy.
Getahun D, Amre DK, Ananth CV, Demissie K, Rhoads GG. 
Temporal changes in rates of stillbirth, neonatal and infant mortality among triplet gestations in the United States. 
Am J Obstet Gynecol. 2006 May 2; [E-pub ahead of print]

Objective: The purpose of this study was to examine temporal changes in stillbirth, neonatal and infant mortality rates among triplet births in the US, and to assess the contributions of triplet delivery at <34 weeks to these changes. Study Design: Data on triplet live births, and fetal and infant deaths (1990-2002) delivered at >/=22 weeks and fetuses weighing >/=500 g (n = 66,986) were derived from the US linked birth/infant death data files. Relative risk (RR), quantifying changes in triplet stillbirth, neonatal (death within the first 28 days) and infant mortality (death within the first year) rates between 1990 and 1991 and 2001 and 2002, were derived. Temporal changes in triplet births at <34 weeks, and changes in stillbirth, and neonatal and infant mortality rates were examined through logistic regression models before and after adjusting for confounders. Results: Triplet births at <34 weeks increased by 25% between 1990 and 1991 (48.7%) and 2001 and 2002 (60.9%). Stillbirth, neonatal and infant mortality rates declined by 52% (RR 0.48, 95% confidence interval [CI] 0.36-0.63), 32% (RR 0.68, 95% CI 0.58-0.80), and 38% (RR 0.62, 95% CI 0.53-0.71), respectively, between 1990 and 1991 and 2001 and 2002. The increase in triplet births at <34 weeks was not associated with the stillbirth decline, but was associated with an excess 14% and 12% increase in neonatal and infant deaths, respectively. Conclusion: Our findings suggest that the increase in triplet births at <34 weeks’ gestation is not associated with changes in triplet stillbirths, but is associated with increases in triplet neonatal and infant mortality.

Cotter AM, Garcia AG, Duthely ML, Luke B, O'Sullivan MJ 
Is antiretroviral therapy during pregnancy associated with an increased risk of preterm delivery, low birth weight, or stillbirth? 

Background: Data on complications of pregnancy associated with antiretroviral therapy are limited. Some small studies have demonstrated an increased preterm delivery rate, but a recent retrospective United States multisite study did not concur with these findings. Our objective was to investigate whether antiretroviral therapy was associated with adverse pregnancy outcome at a single site. Methods: Using prospectively gathered data, women were identified who were determined to be human immunodeficiency virus positive before or during pregnancy who sought care at our prenatal clinic and who gave birth at the University of Miami/Jackson Memorial Medical Center from 1990 through 2002. The outcome measures were preterm delivery, low birth weight, and stillbirth. Results: The cohort included 999 women who received antiretroviral therapy during pregnancy (monotherapy in 492, combination therapy without a protease inhibitor [PI] in 373, and combination therapy with a PI in 134) and 338 women who did not receive therapy. After adjustment for possible confounders, only combination therapy with a PI
was associated with an increased risk of preterm delivery, compared with any other combination (odds ratio, 1.8 [95% confidence interval, 1.1-3.0]). There were no differences in rates of low birth weight and stillbirth, regardless of therapy. Conclusion: Compared with monotherapy and combination therapy without a PI, only combination therapy with a PI was associated with an increased risk of preterm delivery.


St John A, Cooke M, Goopy S.
Shrouds of silence: Three women's stories of prenatal loss.

Objective: To give voice to the experiences of women who have suffered a prenatal loss prior to a full term pregnancy. Design: A descriptive, exploratory qualitative study using mini-biographies was used. In-depth interviews were conducted with women to record their experiences and stories. Interviews were transcribed and the patterns that emerged from the data were identified and themes generated. Subjects: The mini-biographical stories of three women were gathered. Interviews occurred in the women's homes. The women were recruited through an advertisement in the Stillbirth and Neonatal Death Support (SANDS) newsletter. Results: The stories revealed the tragedy, pain and silence endured by these women, as they live with loss and grief. Common themes emerged from their stories highlighting grief, isolation, anger and self-blame in the face of their loss and subsequent full term pregnancy. Conclusions and Implications. For Practice: The emergent theme suggests that further research needs to explore how society and the health care community may compound women's grief and isolation and in-turn perpetuate their feelings of anger. In telling their stories, these women give voice to their current health care practices may be modified to better support the needs of women who have suffered a prenatal loss and also points to the need for further research. Specifically, the study identifies a need for nurses and midwives to offer sensitive care, acknowledgment of previous loss and supportive counseling strategies for women following prenatal loss and during antenatal care for subsequent pregnancies.

Full-text available at: http://www.ingentaconnect.com (not a U.S. Government site)


Objective: We sought to assess whether small for gestational age is a risk factor for stillbirth of a subsequent sibling. Methods: The Missouri maternally linked cohort data set, containing data on births from 1978 through 1997, was used. We identified the study group (women who delivered a SGA infant in the first pregnancy) and a comparison group (women who delivered a non-SGA infant in their first pregnancy) and compared the outcome (stillbirth) in the second pregnancy between both groups. Results: We
analyzed information on the first and second pregnancies of 402,015 women (43,549 [10.8%] in the study arm and 358,466 [89.2%] in the comparison arm). Of the 1,883 cases of stillbirth in the second pregnancy, 314 cases occurred in mothers with a history of SGA (stillbirth rate 7.2/1,000) and 1,569 in the comparison group (stillbirth rate 4.4/1,000), P < .001. The adjusted risk of stillbirth was 60% higher in women with a prior SGA (odds ratio [OR] 1.6, 95% confidence interval [CI] 1.4-1.8). The risk for stillbirth in the second pregnancy increased with decreasing gestational age at birth of the SGA infant in the first pregnancy (term: OR 1.4, 95% CI 1.2-1.6; preterm: OR 2.8, 95% CI 2.0-3.8; and very preterm: OR 4.2, 95% CI 2.4-7.3), P for trend < .001. Conclusion: Small for gestational age is a marker for subsequent stillbirth, and the risk rises with decreasing gestational age of the SGA birth. This information is potentially useful for counseling parents of SGA infants.

Full-text available at http://www.greenjournal.org/cgi/content/full/107/4/851 (not a U.S. Government site)


Systematic audit of stillbirths and neonatal deaths at an institutional and regional level is the first step in the descriptive epidemiology of perinatal mortality and a necessary means for identifying the causes of such deaths. Uniform classification systems within an organizational jurisdiction enable the identification of the major contributing categories, facilitate analysis, and enable consideration of possible interventions and strategies for prevention. This paper describes the application of the classification systems recently developed by the Perinatal Society of Australia and New Zealand (PSANZ), as part of a perinatal audit package, to a cohort of 3485 perinatal deaths in Victoria over a 5-year period, 2000-2004. There are many other perinatal mortality audit systems in place in other jurisdictions, designed to produce the same result, i.e. a better understanding of the causes of perinatal mortality and the possibilities for prevention.


The aim of this study was to assess the recurrent risk of an unexplained stillbirth at term. A total of 75 women who delivered stillbirths were matched for maternal age and parity with 75 controls. After excluding explained stillbirths, matched cases and controls were compared for maternal age, length of gestation, birth weight and 'interval to next birth'. The main outcome measure was the frequency of recurrence of a stillbirth. Both groups were similar for maternal age and length of gestation. Birth weight was marginally different (odds ratio (OR) = 0.997, 95% confidence interval (CI) 0.996, 0.999) and 'interval to next birth' was longer (OR = 1.08, 95% CI 1.00, 1.17). There were no
stillbirths in cases and controls at follow-up. We conclude that a woman who has had an unexplained stillbirth at term has no greater risk of recurrence than a matched control. However, the 'interval to next birth' was significantly longer.

Full-text available at: http://taylorandfrancis.metapress.com (not a U.S. Government site)

Salihu HM, Sharma PP, Ekundayo OJ, Kristensen S, Badewa AP, Kirby RS, Alexander GR.

**Childhood pregnancy (10-14 years old) and risk of stillbirth in singletons and twins.**

Objective: To clarify the association between childhood pregnancy and risk of stillbirth.

Study Design: We analyzed singleton and twin pregnancies that occurred in children (10-14 years old) in the United States from 1989 to 2000. We estimated the absolute and relative risks of stillbirth by using 15- to 19-year-old and 20- to 24-year-old mothers as comparison groups.

Results: The analysis involved 17.8 million singletons and 337,904 individual twins. The rate of stillbirth was highest in pediatric mothers for both singletons (12.8/1000) and twins (56/1000) compared with adolescent (6.8/1000 in singletons and 29/1000 in twins) and mature (5.5/1000 in singletons and 20/1000 in twins) mothers.

After adjusting for confounding characteristics, pediatric mothers continued to exhibit significantly elevated risk for stillbirth in both singletons (odds ratio, 1.57; 95%CI, 1.49-1.66) and twins (odds ratio, 1.97; 95%CI, 1.42-2.73). Preterm birth rather than small size for gestational age was revealed by means of sequential modeling to account for the excess risk of stillbirth observed in pediatric gravidas.

Conclusion: Pregnancy in childhood is a risk factor for stillbirth; shortened gestation rather than reduction in fetal growth is the mediating pathway.


Fellman J, Eriksson AW.

**Stillbirth rates in singletons, twins and triplets in Sweden, 1869 to 2001.**

The temporal variation in the stillbirth rates (SBR), measured as the number of stillborn per 1000 total births, among singletons, twins and triplets was studied on Swedish birth data for the period 1869 to 2001 and comparisons with data from other populations were made. Among both single and multiple births there were marked, almost monotonously decreasing trends in the stillbirth rates. Among singletons the stillbirth rate decreased from 29.5 per 1000 in the period 1869 to 1878 to 3.4 in the period 1991 to 2001. Among twins the stillbirth rate decreased from 94 per 1000 in 1869 to 1878 to a minimum of 8.2 in 1991 to 2001 and among triplets from 166 per 1000 to a minimum of 19.8. The relative declining pattern in the SBRs was almost the same, being 88% among singletons, 91% among twins and 88% among triplets. In the 1980s and 1990s the definition of the stillbirth rate was changed in many countries, including Finland, but no changes in the definition of stillbirths have been made in Sweden. The effect of the artificial reproduction techniques, including in vitro fertilization, on the rates of multiple
maternities is also discussed. It was noted especially that they had a more marked effect on the triplet than on the twinning rate.


Objective: We sought to assess whether small for gestational age is a risk factor for stillbirth of a subsequent sibling. Methods: The Missouri maternally linked cohort data set, containing data on births from 1978 through 1997, was used. We identified the study group (women who delivered a SGA infant in the first pregnancy) and a comparison group (women who delivered a non-SGA infant in their first pregnancy) and compared the outcome (stillbirth) in the second pregnancy between both groups. Results: We analyzed information on the first and second pregnancies of 402,015 women (43,549 [10.8%] in the study arm and 358,466 [89.2%] in the comparison arm). Of the 1,883 cases of stillbirth in the second pregnancy, 314 cases occurred in mothers with a history of SGA (stillbirth rate 7.2/1,000) and 1,569 in the comparison group (stillbirth rate 4.4/1,000), P < .001. The adjusted risk of stillbirth was 60% higher in women with a prior SGA (odds ratio [OR] 1.6, 95% confidence interval [CI] 1.4-1.8). The risk for stillbirth in the second pregnancy increased with decreasing gestational age at birth of the SGA infant in the first pregnancy (term: OR 1.4, 95% CI 1.2-1.6; preterm: OR 2.8, 95% CI 2.0-3.8; and very preterm: OR 4.2, 95% CI 2.4-7.3), P for trend < .001. Conclusion: Small for gestational age is a marker for subsequent stillbirth, and the risk rises with decreasing gestational age of the SGA birth. This information is potentially useful for counseling parents of SGA infants.

Full-text available at: http://www.greenjournal.org/cgi/content/full/107/4/851 (not a U.S. Government site)


Stillbirth remains an important cause of fetal loss in both the term and late-preterm (near-term) pregnancy. As ongoing research further elucidates the causes of intrauterine fetal demise (IUFD), strategies can be tested to reduce its occurrence. Currently, reduction of IUFD in the term and late preterm infants should focus on reduction or elimination of risk factors (eg, smoking and control of medical conditions) and enhanced fetal surveillance in those pregnancies identified to be at increased risk.


Objective: This study was undertaken to characterize risk factors associated with nonanomalous stillborn (SB) infants and to ascribe the probability of fetal survival by gestational age among high-risk pregnancies. Study Design: We compiled a database of all SB infants and an equivalent number of controls using information obtained from Utah Birth and Fetal Death Certificates during the years 1992 through 2002. Adjusted and unadjusted odds ratios for risk factors associated with SB were generated. Cox proportional hazard models were used to generate survival curves comparing pregnancies complicated by chronic hypertension or gestational hypertension with those of controls. Results: Infants with major anomalies were eliminated from both cases and controls, to generate 1566 nonanomalous SBs and 2720 nonanomalous controls. In a logistic regression model controlling for multiple maternal and fetal factors, placental abruption, hydramnios, cord prolapse, and essential hypertension were associated with an increased risk of SB. In pregnancies complicated by essential hypertension, the survival curve diverged from that of controls at those gestational ages approaching term (hazard ratio 2.24; 95% CI 1.52-3.32). Conclusion: SB in nonanomalous infants in Utah is more common among pregnancies complicated by placental abruption, hydramnios, cord prolapse, and essential hypertension.


Bateman BT, Simpson LL.
Higher rate of stillbirth at the extremes of reproductive age: A large nationwide sample of deliveries in the United States.

Objective: The purpose of this study was to assess the effect of maternal age on the rate of stillbirth in a large, nationwide sample of deliveries in the United States. Study Design: Data were derived from the Nationwide Inpatient Sample for the years 1995 through 2002. With the use of ICD-9 codes, the rate of stillbirth was determined as a function of maternal age. Multivariate regression analysis was used to assess the effect of maternal age on the odds of stillbirth, with adjustment for multiple known risk factors for stillbirth. Results: There were 5,874,203 deliveries that were identified for analysis. The unadjusted rate of stillbirth was elevated for teenagers and for women aged \( \geq 35 \) years. In the multivariate analysis, compared with women 20 to 34 years old, women who were \(< 19\) years old were more likely to have a pregnancy outcome of stillbirth (odds ratio, 1.11; 95% CI, 1.08-1.14), as were women who were 35 to 39 years old (odds ratio, 1.28; 95% CI, 1.24-1.32) and women who were \( \geq 40 \) years old (odds ratio, 1.72; 95% CI, 1.63-1.81). Conclusion: The extremes of maternal age are associated with an increased risk for stillbirth, even after adjustment for a large number of known predisposing conditions.


Becher JC, Bell JE, Keeling JW, Liston WA, McIntosh N, Wyatt B.
The Scottish Perinatal Neuropathology Study--clinicopathological correlation in stillbirths.
BJOG. 2006 Mar; 113(3):310-7.

Objective: To examine the neuropathology of fetuses dying before birth, to determine the timing of any brain damage seen and to ascertain clinical associations of pre-existing brain damage. Design: Population-based observational study. Setting: All 22 delivery units within Scotland, 1995-1998. Sample: All stillborn fetuses > or =24 weeks of gestation excluding those with chromosomal abnormality or central nervous system/cardiothoracic malformation. Methods: Clinical detail was collected on all stillborn fetuses. Requests for postmortem included separate request for detailed neuropathological examination. Stillborn fetuses were classified as full term antepartum (normal growth/growth restricted), preterm antepartum (normal growth/growth restricted), intrapartum (full term/preterm), multiple births and stillborn fetuses following abruptions. Clinicopathological correlation attempted to define the timing of brain insult. Placentas were examined for each case where available. Main Outcome Measures: Presence of established and/or recent brain damage. Results: Clinical details were available for 471 stillborn fetuses, and detailed neuropathology was possible in 191 cases. Of these 191, 13 were multiple births, 9 died following abruption, 12 were intrapartum deaths and 157 were antepartum stillborn fetuses (99 preterm and 58 full term). Recent or established brain damage was seen in 66% of the entire cohort. Thirty-five percent of all cases showed well-established hypoxic damage predating the last evidence of fetal life, and this was more common in preterm fetuses (P = 0.015), those fetuses with evidence of recent damage (P < 0.001), in pregnancies complicated by pregnancy-induced hypertension (P = 0.044) and those in whom the placenta was <10th centile (P = 0.002). Conclusions: Brain damage is commonly seen in stillborn infants, and in around one-third of cases, damage predates the period immediately before death. Factors suggesting suboptimal placental function are associated with such damage. Early identification of placental impairment may lead to improved pregnancy outcome.


Barr P.
Relation between grief and subsequent pregnancy status 13 months after perinatal bereavement.

Aims: The present longitudinal study sought to explore the relationship between parental grief following perinatal bereavement and subsequent pregnancy, according to the particular facets of grief and pregnancy state being considered. Method: The study participants were 63 couples who had been bereaved by stillbirth (n = 31) or neonatal death (n = 32). The relationship of self-reported grief (Perinatal Grief Scale-33 Active Grief, Difficulty Coping and Despair) 1 month and 13 months after the loss to subsequent pregnancy status (Pregnant, n = 20, Live Baby, n = 10, Trying, n = 11, Not Trying, n = 22) at 13 months was investigated with repeated measures analysis of variance. Results:
There were statistically significant main effects for Active Grief and Difficulty Coping in women and men and Despair in women, but not in men. There was a statistically significant Active Grief by pregnancy status interaction in women (F(3, 59) = 2.89, P = 0.04), but not in men. Simple main effects analysis indicated a statistically significant decrease in Active Grief in women who were pregnant (F(1, 59) = 52.8, P < 0.0005), women who were not pregnant and not trying to conceive (F(1, 59) = 27.5, P < 0.0005), and women who had had a live baby (F(1, 59) = 9.62, P = 0.003). There was no statistically significant decrease in Active Grief in women who were not pregnant but trying to conceive (F(1, 59) = 3.44, P = 0.07). The Difficulty Coping in women and men and Despair in women by pregnancy status interactions were not statistically significant. None of the between-subjects main effects for pregnancy status was statistically significant in women or men. Conclusion: The relation between grief and subsequent pregnancy differed with the sex of the parent and the particular facets of grief and pregnancy state being considered. Subsequent pregnancy was related to Active Grief in women, but not to Difficulty Coping or Despair that are known to be predictors of chronic grief.

Full-text available at: http://www.atypon-link.com (not a U.S. Government site)

Psychological impact of stillbirth on fathers in the subsequent pregnancy and puerperium.

Background: Approximately 1 in 200 UK pregnancies ends in stillbirth. Although serious psychological effects of stillbirth on mothers are well established, much less is known about the impact of such loss on fathers. Aims: To assess the psychological morbidity of fathers in the pregnancy and post-partum year subsequent to a stillbirth, to test within-couple effects and to identify risk factors. Method: This was a community-based cohort study of 38 pregnant couples whose previous pregnancy had ended in stillbirth, and 38 pair-matched controls. Psychological assessments took place antenatally and at 6 weeks, 6 months and 1 year postnatally. Results: Fathers in the index group experienced significant levels of anxiety and post-traumatic stress disorder antenatally, but all of their symptoms remitted postnatally (after the birth of a live baby). Fathers' symptom levels were lower than those of mothers at all time points. In contrast to mothers, fathers experienced greater anxiety when a subsequent pregnancy (following stillbirth) was delayed. Conclusions: The vulnerability of fathers to psychological distress during the pregnancy after a stillbirth needs to be recognized.

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Sharma PP, Salihu HM, Oyelese Y, Ananth CV, Kirby RS
Is race a determinant of stillbirth recurrence?.

Background: A history of stillbirth may result in an increased risk for recurrence, although information regarding this remains scanty. It is also uncertain whether race is a
determinant of stillbirth recurrence given that the risk of stillbirth varies across racial and ethnic populations. Methods: The Missouri maternally linked cohort data set containing births from 1978 through 1997 was used. We identified the study group (women who experienced a stillbirth in the first pregnancy) and a comparison group (women who delivered a live birth in their first pregnancy) and compared the outcome (stillbirth) in the second pregnancy between the 2 groups. Results: We analyzed 404,180 women with information on first and second pregnancies (1,979 [0.5%] in the study arm, and 402,201 [99.5%] in the comparison arm). Of the 1,929 cases of stillbirths in the second pregnancy, 45 cases occurred in mothers with a history of stillbirth (stillbirth rate = 22.7/1000) and 1,884 in the comparison group (stillbirth rate 4.7/1000, P < .001). The adjusted risk of stillbirth was almost 5-fold as high in women with a prior stillbirth (odds ratio 4.7, 95% confidence interval 3.3-6.6). Analysis across racial groups revealed that whites had lower absolute risk for stillbirth recurrence than African Americans (19.1/1,000 compared with 35.9/1,000, P < .05). The elevated stillbirth recurrence risk was confirmed after adjusting for potential confounders (odds ratio 2.6, 95% confidence interval 1.2-5.7). Conclusion: History of stillbirth is associated with a 5-fold increase for subsequent stillbirth. The recurrence of stillbirth is almost tripled in African Americans as compared with whites.

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Objective: We examine the association between prior cesarean delivery and risk of stillbirth in a subsequent pregnancy. Methods: The Missouri maternally linked cohort data set containing births from 1978 through 1997 was used. We identified a cohort of women who delivered live births by cesarean delivery and a comparison cohort of women who delivered live births vaginally in their first pregnancies. We then compared the risks of stillbirth in the second pregnancy between the 2 groups. Results: We analyzed 396,441 women with information on first and second pregnancies, comprising 71,950 (18.1%) in the cesarean arm, and 324,491 (81.9%) in the vaginal birth arm. Rates of stillbirth among women with and those without history of cesarean delivery were 4.4 and 4.1 per 1,000 births, respectively (P = .2). The adjusted estimates also showed no difference in risk for stillbirth between the 2 groups (odds ratio [OR] 1.1, 95% confidence interval [CI] 1.0-1.3). Among whites, the stillbirth rates in women with and those without history of cesarean delivery were 3.7 and 3.6 per 1,000 births, respectively (OR 1.0, 95% CI 0.9-1.2). Among blacks, both the absolute and the adjusted relative risks for stillbirth were elevated in mothers with history of cesarean delivery (stillbirth rate 9.3 versus 6.8 per 1,000 births; OR 1.4, 95% CI 1.1-1.7). Conclusion: Overall, our analysis did not detect an association between cesarean history and subsequent stillbirth. However, cesarean delivery may increase the risk for subsequent stillbirth among black mothers, a group with the highest cesarean delivery rate in the country.

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Background: Stillbirth rate is an important indicator of access to and quality of antenatal and delivery care. Obtaining overall estimates across various regions of the world is not straightforward due to variation in definitions, data collection methods and reporting.

Methods: We conducted a systematic review of a range of pregnancy-related conditions including stillbirths and performed meta-analysis of the subset of studies reporting stillbirth rates. We examined variation across rates and used meta-regression techniques to explain observed variation. Results: We identified 389 articles on stillbirth prevalence among the 2580 included in the systematic review. We included 70 providing 80 data sets from 50 countries in the meta-analysis. Pooled prevalence rates show variation across various subgroup categories. Rates per 100 births are higher in studies conducted in less developed country settings as compared to more developed (1.17 versus 0.50), of inadequate quality as compared to adequate (1.12 versus 0.66), using sub-national sample as compared to national (1.38 versus 0.68), reporting all stillbirths as compared to late stillbirths (0.95 versus 0.63), published in non-English as compared to English (0.91 versus 0.59) and as journal articles as compared to non-journal (1.37 versus 0.67). The results of the meta-regression show the significance of two predictor variables - development status of the setting and study quality - on stillbirth prevalence. Conclusion: Stillbirth prevalence at the community level is typically less than 1% in more developed parts of the world and could exceed 3% in less developed regions. Regular reviews of stillbirth rates in appropriately designed and reported studies are useful in monitoring the adequacy of care. Systematic reviews of prevalence studies are helpful in explaining sources of variation across rates. Exploring these methodological issues will lead to improved standards for assessing the burden of reproductive ill-health.

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Tomashek KM, Ananth CV, Cogswell ME.
Risk of stillbirth in relation to maternal haemoglobin concentration during pregnancy.

The authors determined the association between maternal haemoglobin concentration measured at <28 weeks' gestation and late fetal death at >or=28 weeks' gestation (stillbirth). Data were derived from the National Maternal and Infant Health Survey--a nationally representative survey of US deliveries in 1988. Analysis was restricted to women with a singleton live birth (n = 4,199) or a stillbirth (n = 1,375) for whom maternal prenatal care, haemoglobin, smoking status and gestational age data were available. Haemoglobin concentrations during first and second trimesters, respectively, were classified as mild (10.0 to <11.0 and 9.5 to <10.5 g dL(-1)) or moderate (9.0 to <10.0 and 8.5 to <9.5 g dL(-1)) anaemia, or high haemoglobin (>or=14.6 g dL(-1) in either trimester). Hazard ratios (HR) and 95% confidence intervals (CI) for stillbirth were
derived from discrete proportional hazards regression models after adjusting for confounders. Stillbirth was not associated with mild anaemia or high haemoglobin in either the first or second trimester of pregnancy. Moderate anaemia measured before 28 weeks' gestation was significantly associated with an increased risk of stillbirth among non-black women (adjusted HR: 4.4; 95% CI: 1.02, 19.01). Moderate anaemia was not associated with stillbirths among black women. Further investigation regarding causal mechanisms for this association is warranted.


Objective: To describe the association between pregnancy associated plasma protein A (PAPP-A), alpha-fetoprotein (AFP) and adverse perinatal outcome. Methods: We conducted a multicenter prospective cohort study of 8,483 women attending for prenatal care in southern Scotland between 1998 and 2000. The risk of delivering a small for gestational age infant, delivering preterm, and stillbirth were related to maternal serum levels of PAPP-A and AFP. Results: Women with a low PAPP-A were not more likely to have elevated levels of AFP. Compared with women with a normal PAPP-A and a normal AFP, the odds ratio for delivering a small for gestational age infant for women with a high AFP was 0.9 (95% confidence interval [CI] 0.5-1.6), for women with a low PAPP-A was 2.8 (95% CI 2.0-4.0), and for women with both a high AFP and a low PAPP-A was 8.5 (95% CI 3.6-20.0). The odds ratio for delivering preterm for women with a high AFP was 1.8 (95% CI 1.3-2.7), for women with a low PAPP-A was 1.9 (95% CI 1.3-2.7), and for women with both a low PAPP-A and a high AFP was 9.9 (95% CI 4.4-22.0). These interactions were statistically significant for both outcomes (P = .03 and .04, respectively). There was a nonsignificant trend toward a similar interaction in relation to stillbirth risk. Of the women with the combination of a low PAPP-A and high AFP, 32.1% (95% CI 15.9-52.4) delivered a low birth weight infant. Conclusion: Low maternal serum levels of PAPP-A between 10 and 14 weeks and high levels of AFP between 15 and 21 weeks gestation are synergistically associated with adverse perinatal outcome.

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Background: Maternal cigarette smoking has been causally associated with an increased risk for stillbirth. Preliminary reports suggest an increased risk for stillbirth with smokeless tobacco use during pregnancy. Methods: We conducted a population-based prospective cohort study to investigate this association by using a house-to-house approach to recruit 1,217 women who were between 3 and 7 months' gestation. Of these,
96% were contacted after delivery to determine the pregnancy outcome. Demographic and maternal variables which were apparently associated either with stillbirth or with smokeless tobacco use (OR >or= 1.5) were included as potential confounders. Stillbirth was defined as any delivery of a dead fetus after 20 completed weeks of gestation. We used time-to-event methods to analyze the risk of stillbirth. Results: Overall occurrence of stillbirth among singleton deliveries in this population was 4.1%. Smokeless tobacco use was reported by 17% of women; 8.9% of smokeless tobacco users had a stillbirth compared with 3.1% among nonusers (life-table adjusted hazard ratio = 3.1; 95% confidence interval = 1.7-5.6). After adjustment by the Cox proportional hazards procedure for age, educational and socioeconomic background, working status of mother, parity, prenatal care variables, and place of delivery, the risk for stillbirth in users was 2.6 (95% confidence interval-1.4-4.8). Most women used mishri (a pyrolyzed tobacco product often used as dentifrice), and there was a dose-response relationship between the daily frequency of use and stillbirth risk. The risk of stillbirth associated with smokeless tobacco use was greater in earlier gestational periods. Conclusions: Smokeless tobacco use during pregnancy increases stillbirth risk, with a risk at least as great as that associated with maternal cigarette smoking.

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Smoke from biomass combustion produces some of the same pollutants found in tobacco smoke and ambient air, yet only one study to date has linked cooking with biomass fuels to increased risk of stillbirth. The mechanisms by which biomass smoke may cause stillbirth are through exposure to CO and particulates in biomass smoke. Using information on 19,189 ever-married women aged 40-49 included in India's 1998-99 National Family Health Survey, we examined the association between household use of biomass fuels (wood, dung, and crop residues), tobacco smoke (both active and passive), and risk of stillbirth. Data were analyzed using binary and multinomial logistic regression after controlling for several potentially confounding factors. Results indicate that, with other factors controlled, women who cook with biomass fuels are significantly more likely to have experienced a stillbirth than those who cook with cleaner fuels (OR= 1.44; 95% CI: 1.04, 1.97). Women who cook with biofuels are twice as likely to have experienced two or more stillbirths as those who cook with cleaner fuels (RRR= 2.01; 95% CI: 1.11, 3.62). The adjusted effect of active tobacco smoking is also positive (OR = 1.23) but not statistically significant. No effect of passive smoking was found, nor was there evidence of any modifying effects of tobacco smoking.

Full-text available at: http://taylorandfrancis.metapress.com (not a U.S. Government site)

Objective: This is a systematic review of the literature on the causes of stillbirth and clinical opinion regarding strategies for its prevention. Study Design: We reviewed the causes of stillbirth by performing a Medline search limited to articles in English published in core clinical journals from January 1, 1995, to January 1, 2005. Articles before this date were included if they added historical information relevant to the topic. A total of 1445 articles obtained, 113 were the basis of this review and chosen based on the criterion that stillbirth or fetal death was central to the article. Results: Fifteen risk factors for stillbirths were identified and the prevalence of these conditions and associated risks are presented. The most prevalent risk factors for stillbirth are prepregnancy obesity, socioeconomic factors, and advanced maternal age. Biologic markers associated with increased stillbirth risk are also reviewed, and strategies for its prevention identified.

Conclusion: Identification of risk factors for stillbirth assists the clinician in performing a risk assessment for each patient. Unexplained stillbirths and stillbirths related to growth restriction are the 2 categories of death that contribute the most to late fetal losses. Late pregnancy is associated with an increasing risk of stillbirth, and clinicians should have a low threshold to evaluate fetal growth. The value of antepartum testing is related to the underlying risk of stillbirth and, although the strategy of antepartum testing in patients with increased risk will decrease the risk of late fetal loss, it is of necessity associated with higher intervention rates.


Objectives: We examined age, period, and cohort (APC) effects on temporal trends in stillbirths among Black and White women in the United States. Methods: We conducted a cohort study of Black and White women who delivered a singleton live-born or stillborn infant during 1981 through 2000. We analyzed stillbirth rates at 20 or more weeks of gestation within 7 age groups, 4 periods, and 10 "central" birth cohorts after adjusting for confounders. Results: In both racial groups, women younger than 20 years or 35 years or older were at increased risk of stillbirth; risks decreased over successive periods in all age groups. Birth cohort had no impact on stillbirth trends among Blacks and only a small, non significant effect among Whites. Analyses of various APC combinations showed that Blacks were at a 1.2- to 2.9-fold increased risk for stillbirth relative to Whites. Attributable fractions for stillbirth because of age, period, and cohort effects were 16.5%, 24.9%, and 0.1%, respectively, among Black women and 14.5%, 36.2%, and 2.1%, respectively, among White women. Conclusions: Strong effects of age and period were observed in stillbirth trends, but these factors do not explain the persistent stillbirth disparity between Black and White women.

Full-text available at: http://www.ajph.org/cgi/content/full/95/12/2213 (not a U.S. Government site)

Astolfi P, De Pasquale A, Zonta L.
Late childbearing and its impact on adverse pregnancy outcome: Stillbirth, preterm delivery and low birth weight.

Background: The role of parental ageing on the incidence of adverse pregnancy outcome is based on increased morbidity and obstetric problems during pregnancy and delivery in old mothers, and on the accumulation of spontaneous harmful mutations for continuous cell divisions during spermatogenesis in old fathers. The aim of this study is to estimate the impact of paternal and maternal ageing on the risk of adverse pregnancy outcome.

Data and Methods: From the group of 3,616,622 Italian singletons born in 1990-1996 we estimated the risks of stillbirth, preterm birth (<37 weeks of gestation) in live births, and low birth-weight (< 2.3 Kg) in live full-term births. The risks were estimated as a function of maternal and paternal ageing through logistic regression models, which included, as covariates, parity (1st, 2nd, > or =3rd) and family education (low, < or =8 years of schooling for both parents; high, >8 years for at least one parent). Parental ages were examined as quantitative (in one year classes) or categorical factors (in three classes: fathers 20-29, 30-39, > or =40; mothers 20-29, 30-34, > or =35).

Results and Conclusions: We found that, compared with 20-29-year old parents, mothers > or =30 years and fathers > or =40 years are at risk of adverse pregnancy outcome. The effects are more relevant for preterm births and greater in the least than in the most favourable birth conditions, i.e., in first-born children of less educated families than in second-born children of highly educated families. For the risk of a preterm delivery, the odds ratio is OR = 1.32 [1.28-1.36] in mothers aged 30-34 years, and OR=1.97 [1.88-2.07] in mothers 235 years in the least favourable conditions, and OR = 1.14 [1.10-1.18] and OR = 1.56 [1.22-1.27] respectively, in the most favourable conditions. The impact of paternal ageing is smaller but significant in fathers > or =40 years: for the risk of a preterm birth, the odds ratio is OR = 1.40 [1.33-1.47] in the least favourable conditions, and OR = 1.14 [1.08-1.21] in the most favourable conditions. This last, baseline risk might be indicative of a paternal genetic component associated with childbearing in advanced age.

Classification of stillbirth by relevant condition at death (ReCoDe): Population based cohort study.

Objective: To develop and test a new classification system for stillbirths to help improve understanding of the main causes and conditions associated with fetal death. Design: Population based cohort study. Setting: West Midlands region. Subjects: 2625 stillbirths from 1997 to 2003. Main Outcome Measures: Categories of death according to conventional classification methods and a newly developed system (ReCoDe, relevant condition at death). Results: By the conventional Wigglesworth classification, 66.2% of the stillbirths (1738 of 2625) were unexplained. The median gestational age of the unexplained group was 237 days, significantly higher than the stillbirths in the other categories (210 days; P < 0.001). The proportion of stillbirths that were unexplained was high regardless of whether a postmortem examination had been carried out or not (67% and 65%; P = 0.3). By the ReCoDe classification, the most common condition was fetal
growth restriction (43.0%), and only 15.2% of stillbirths remained unexplained. ReCoDe identified 57.7% of the Wigglesworth unexplained stillbirths as growth restricted. The size of the category for intrapartum asphyxia was reduced from 11.7% (Wigglesworth) to 3.4% (ReCoDe). Conclusion: The new ReCoDe classification system reduces the predominance of stillbirths currently categorised as unexplained. Fetal growth restriction is a common antecedent of stillbirth, but its high prevalence is hidden by current classification systems. This finding has profound implications for maternity services, and raises the question whether some hitherto "unexplained" stillbirths may be avoidable.

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Objective: We estimate the impact of increasing fetal number on fetal and infant mortality among Hispanic mothers. Methods: Retrospective cohort study involving singletons, twins, and triplets delivered in the United States from 1995 through 2000, except for the analysis on infant mortality in singletons (1995 through 1999). Main outcome measures were stillbirth (> or = 20 weeks) and infant mortality (< 365 days). Results: A total of 37,489,600 individual births were reviewed, consisting of 36,840,704 singletons, 613,930 twins, and 34,966 triplets. Hispanics accounted for 6,848,027 (18.6%) singletons, 85,887 (14.0%) individual twins, and 2,725 (7.8%) individual triplets. Among singletons, stillbirth (odds ratio [OR] 0.91, 95% confidence interval [CI] 0.90-0.92) and infant mortality (OR 0.85, 95% CI 0.84-0.86) were both lower in Hispanics than in whites. Among twins, Hispanics had a lower risk for infant mortality (OR 0.93, 95% CI 0.88-0.97) but a comparable risk for stillbirth (OR 1.06, 95% CI 0.98-1.13). Although the risk for infant mortality in Hispanic triplets was comparable to that of whites (OR 1.20, 95% CI 0.94-1.54), Hispanic triplets had a 50% higher likelihood of dying in utero (OR 1.50, 95% CI 1.06-2.14). Conclusion: Although Hispanic infants generally show better or comparable survival indices compared with whites, the risk for fetal and infant death in Hispanics increases in fetal number in a dose-dependent fashion, thereby obliterating the Hispanic advantage. The elevated risk for stillbirth among Hispanic triplets is particularly noteworthy and underscores the need for caution in making generalizations of favorable birth outcomes in Hispanics.

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Objective: We examined the relationship between extreme parity and risk for stillbirth in the United States. Methods: Singleton deliveries at 20 weeks of gestation or later in the
United States from 1989 through 2000 were analyzed. Risk for stillbirth in women with 1-4 (moderate parity, category I), 5-9 (high parity, category II), 10-14 (very high parity, category III), and 15 or more (extremely high parity, category IV) prior live births were computed using logistic regression. Results: Overall, 27,069,385 births, including 1,206 to extremely high parity mothers, were analyzed. Of the 81,386 stillbirths, 71,623 (2.8/1,000), 9,206 (5.0/1,000), 531 (14.4/1,000), and 26 (21.6/1,000) cases occurred among category I, category II, category III, and category IV gravidas, respectively. With category I as referent category, the odds ratio for stillbirth increased consistently with ascending parity after adjusting for potential confounders: category II (odds ratio [OR] 1.05, 95% confidence interval [CI] 1.02-1.07), category III (OR 1.97, 95% CI 1.81-2.15), and category IV (OR 2.31, 95% CI 1.56-3.42) (P for trend < .001). Among extremely high parity women (category IV), the odds ratio for stillbirth also increased with unit increment in the number of prior live births: 15 (OR 2.72, 95% CI 1.29-5.74), 16 (OR 3.14, 95% CI 1.17-8.41), 17 (OR 6.11, 95% CI 2.56-16.5), and 18 or more prior live births (OR 16.17, 95% CI 8.77-29.82) (P for trend < .001). Conclusions: The risk for stillbirth is substantially elevated among very high and extremely high parity women, and care providers may consider these groups for targeted periconceptional counseling.

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Pasupathy D, Smith GC.  
**The analysis of factors predicting antepartum stillbirth.**  

Antepartum stillbirth is the single most common cause of perinatal death. Antepartum stillbirth is associated with fetal abnormality, congenital infection, rhesus isoimmunisation, maternal medical conditions, and complications of pregnancy, such as pre-eclampsia and placental abruption. However, the majority have no direct obstetric cause and are referred to as unexplained. Many of these so-called unexplained deaths are associated with growth restriction. Maternal characteristics, such as age and smoking, are associated with an increased risk of antepartum stillbirth. The risk of stillbirth in late pregnancy is related to the function of the placenta in early pregnancy. Placental function can be assessed using circulating markers in the mothers blood, such as pregnancy associated plasma protein A and alpha-fetoprotein. Invasion of the trophoblast into the uterine vessels is associated with decreased resistance to flow in the uterus and impaired placentation is reflected in high resistance Doppler flow velocity waveforms in the utero-placental circulation. Both circulating placental markers and Doppler indices of resistance to flow are predictive of the risk of antepartum stillbirth. However, none of these tools has sufficient positive predictive value to justify population based screening. Future research in unexplained stillbirth should be directed towards developing better predictive tests to identify women at high risk and the evaluation of interventions in large scale trials.

Khodakaram-Tafti A, Ikede BO.  
**A retrospective study of sporadic bovine abortions, stillbirths, and neonatal abnormalities in Atlantic Canada, from 1990 to 2001.**
In a retrospective study on 265 cases of sporadic bovine abortions, stillbirths, and neonatal deaths in Atlantic Canada (1990 to 2001), an etiological diagnosis was made in 117 cases (44.2%). The cases were divided into 2 groups: 234 abortions, and 31 stillbirths and neonatal deaths. Identified causes of abortion were bacteria (24.4%), fungi (6.8%), viruses (6.0%), protozoa (Neospora spp.) (2.1%), congenital anomalies (0.4%), and miscellaneous conditions (1.3%). In addition, placentitis without demonstrable infectious agents was observed in 17 (7.3%). Of the 31 cases of stillbirth and neonatal death, identified causes were dystocia (22.5%), congenital anomalies (22.5%), meconium aspiration syndrome (16.1%), and miscellaneous conditions (6.5%). No etiological diagnosis was made in 59% of abortions and 32.4% of stillbirths and neonatal deaths. The 3 most common identifiable causes of abortion in this study were bacterial, fungal, and viral infections.

Lawn J, Shibuya K, Stein C.

No cry at birth: Global estimates of intrapartum stillbirths and intrapartum-related neonatal deaths.


Objective: Fewer than 3% of 4 million annual neonatal deaths occur in countries with reliable vital registration (VR) data. Global estimates for asphyxia-related neonatal deaths vary from 0.7 to 1.2 million. Estimates for intrapartum stillbirths are not available. We aimed to estimate the numbers of intrapartum-related neonatal deaths and intrapartum stillbirths in the year 2000. Methods: Sources of data on neonatal death included: vital registration (VR) data on neonatal death from countries with full (> 90%) VR coverage (48 countries, n = 97,297); studies identified through literature searches (> 4000 abstracts) and meeting inclusion criteria (46 populations, 30 countries, n = 12,355). A regression model was fitted to cause-specific proportionate mortality data from VR and the literature. Predicted cause-specific proportions were applied to the number of neonatal deaths by country, and summed to a global total. Intrapartum stillbirths were estimated using median cause-specific mortality rate by country (73 populations, 52 countries, n = 46,779) or the subregional median in the absence of country data. Findings: Intrapartum-related neonatal deaths were estimated at 0.904 million (uncertainty 0.65-1.17), equivalent to 23% of the global total of 4 million neonatal deaths. Country-level model predictions compared well with population-based data sets not included in the input data. An estimated 1.02 million intrapartum stillbirths (0.66-1.48 million) occur annually, comprising 26% of global stillbirths. Conclusion: Intrapartum-related neonatal deaths account for almost 10% of deaths in children aged under 5 years. Intrapartum stillbirths are a huge and invisible problem, but are potentially preventable. Programmatic attention and improved information are required.

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Background: Independently of the fetal death cause the beginning and course of stillbirth is closely related with the growing cytotoxic activity at the maternal-fetal interface. RCAS1 participates in the inhibition of maternal immune response during pregnancy. The alterations of RCAS1 protein expression in placental cells seem to determine the beginning of the labor and participate in the placental abruption. The aim of the present study was to investigate RCAS1 expression in placentas obtained following stillbirths or normal term births. Methods: RCAS1 expression was evaluated by Western blot method with the use of monoclonal anti-RCAS1 antibody in 67 placental tissue samples. Pregnant women were divided into four groups according to the mode of labor onset--spontaneous or induced, and the type of labor, stillbirth or labor at term. Placental beta-Actin expression was chosen as a control protein. Relative amounts of placental RCAS1 were compared with the use of Student's t-test, whereas beta-Actin control data were compared with the use of Mann-Whitney U test. Results: The average relative amount of RCAS1 was significantly lower in women with induced stillbirths than in women with induced labor at term. Similarly, significantly lower RCAS1 placental levels were observed in patients with spontaneous stillbirths than in women with spontaneous labor at term. Significant differences in RCAS1 expression were also observed with the respect to the beginning of the stillbirth: spontaneous and induced. Lowest RCAS1 placental levels were observed in women with spontaneous stillbirth. Conclusions: These preliminary results indicate that the alterations of RCAS1 expression in the human placenta may be involved in the changes of maternal immune system that take place during stillbirth.


Background: Death of an infant in utero or at birth has always been a devastating experience for the mother and of concern in clinical practice. Infant mortality remains a challenge in the care of pregnant women worldwide, but particularly for developing countries and the need to understand contributory factors is crucial for addressing appropriate perinatal health. Methods: Using information available in obstetric records for all deliveries (17,072 births) at Harare Maternity Hospital, Zimbabwe, we conducted a cross-sectional retrospective analysis of a one-year data, (1997-1998) to assess demographic and obstetric risk factors for stillbirth and early neonatal death. We estimated risk of stillbirth and early neonatal death for each potential risk factor. Results:
The annual frequency of stillbirth was 56 per 1,000 total births. Women delivering stillbirths and early neonatal deaths were less likely to receive prenatal care (adjusted relative risk [RR] = 2.54; 95% confidence intervals [CI] 2.19-2.94 and RR = 2.52; 95% CI 1.63-3.91), which for combined stillbirths and early neonatal deaths increased with increasing gestational age (Hazard Ratio [HR] = 3.98, HR = 7.49 at 28 and 40 weeks of gestation, respectively). Rural residence was associated with risk of infant dying in utero, (RR = 1.33; 95% CI 1.12-1.59), and the risk of death increased with increasing gestational age (HR = 1.04, HR = 1.69, at 28 and 40 weeks of gestation, respectively). Older maternal age was associated with risk of death (HR = 1.50; 95% CI 1.21-1.84). Stillbirths were less likely to be delivered by Cesarean section (RR = 0.64; 95% CI 0.51-0.79), but more likely to be delivered as breech (RR = 4.65; 95% CI 3.88-5.57, as were early neonatal deaths (RR = 3.38; 95% CI 1.64-6.96). Conclusion: The frequency of stillbirth, especially macerated, is high, 27 per 1000 total births. Early prenatal care could help reduce perinatal death linking the woman to the health care system, increasing the probability that she would seek timely emergency care that would reduce the likelihood of death of her infant in utero. Improved quality of obstetric care during labor and delivery may help reduce the number of fresh stillbirths and early neonatal deaths.

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Sander CM, Gilliland D, Richardson A, Foley KM, Fredericks J.
**Stillbirths with placental hemorrhagic endovasculitis: A morphologic assessment with clinical implications.**

Context: Hemorrhagic endovasculitis (HEV) is a vasodisruptive alteration affecting fetal-placental blood vessels of all calibers. Hemorrhagic endovasculitis is found in association with stillbirth and abnormalities of growth and development in livebirths. The role of HEV in the pathogenesis of these conditions is not known. Objective: To further understand these events, we compare clinicopathologic features of HEV-affected placentas from stillbirths with those from livebirth pregnancies. Additionally, we assess the relationship of morphologic forms of HEV to clinical events and time of fetal death in utero and evaluate the significance of extensive versus localized HEV lesions in placentas of stillbirths. Design: We reviewed the clinical records and slides from 119 stillbirths with placentas affected by HEV classified above a specified severity level (cases) and 119 matched stillbirths with placentas not affected by HEV (controls). A subset of 21 stillbirth placentas exhibiting focal HEV lesions was similarly evaluated. Slides were graded for HEV, villitis of unknown etiology, chorionic thrombi, villous fibrosis, erythroblastosis, and lesions indicative of maternal hypertension. Hemorrhagic endovasculitis was subcategorized into active, bland, and healed forms and clustered capillary lesions (hemorrhagic villitis). Focal, segmental, and diffuse patterns of villous fibrosis were delineated. Interlesional relationships were established by matching HEV severity indices with severity indices of co-existing lesions. Timing of fetal death was determined by published criteria. Data were analyzed for significance using chi2 and t tests. Results were compared with published analyses of livebirths with placental HEV.
Results: Lesions occurring with significant frequency in HEV-affected (case) placentas include villitis of unknown etiology, chorionic thrombi, villous fibrosis, erythroblastosis, and meconium staining. Interlesional relationships were evident between HEV and villous fibrosis, villitis of unknown etiology, and chorionic thrombi. Growth restriction was more common in case versus control infants (P = .02). A segmental pattern of villous fibrosis predominated in cases versus controls and within the case group (P < .001). Time to delivery after fetal death was longer in cases than controls. Active-vasodestructive forms of HEV correlate with shorter intervals of intrauterine retention, whereas bland forms correlate with longer intervals (P = .04). Placentas with focal HEV were associated with coexisting chorionic thrombi and villous fibrosis but not with fetal growth restriction. Conclusions: Patterns of interlesional interplay are similar in HEV-affected placentas of livebirths and stillbirths. This suggests that the pathogenesis of infant morbidity and mortality is similar in both groups. Active-vasodestructive forms of HEV may precede whereas bland forms may follow intrauterine demise. The segmental pattern of villous fibrosis and high incidences of growth restriction, erythroblastosis, and meconium in cases suggests a chronicity of adverse intrauterine events that may precede fetal loss. Stillbirths with focal HEV lesions are probably not at risk.

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Objective: To evaluate the association between maternal pre-pregnancy body mass index (BMI) and the risk of stillbirth and neonatal death and to study the causes of death among the children. DESIGN: Cohort study of pregnant women receiving routine antenatal care in Aarhus, Denmark. Setting: Aarhus University Hospital, Denmark, 1989-1996. POPULATION: A total of 24,505 singleton pregnancies (112 stillbirths, 75 neonatal deaths) were included in the analyses. Methods: Information on maternal pre-pregnancy weight, height, lifestyle factors and obstetric risk factors were obtained from self-administered questionnaires and hospital files. We classified the population according to pre-pregnancy BMI as underweight (BMI <18.5 kg/m(2)), normal weight (BMI 18.5-24.9 kg/m(2)), overweight (BMI 25-29.9 kg/m(2)) and obese (BMI 30.0 kg/m(2) or more). Main Outcome Measures: Stillbirth and neonatal death and causes of death. Results: Maternal obesity was associated with a more than doubled risk of stillbirth (odds ratio = 2.8, 95% confidence interval [CI]: 1.5-5.3) and neonatal death (odds ratio = 2.6, 95% CI: 1.2-5.8) compared with women of normal weight. No statistically significantly increased risk of stillbirth or neonatal death was found among underweight or overweight women. Adjustment for maternal cigarette smoking, alcohol and caffeine intake, maternal age, height, parity, gender of the child, years of schooling, working status and cohabitation with partner did not change the conclusions, nor did exclusion of women with hypertensive disorders or diabetes mellitus. No single cause of death explained the higher mortality in children of obese women, but more stillbirths were caused by unexplained intrauterine death and fetoplacental dysfunction among obese women compared with normal weight women. Conclusion: Maternal obesity more than doubled the risk of
stillbirth and neonatal death in our study. The present and other studies linking maternal obesity to an increased risk of severe adverse pregnancy outcomes emphasize the need for public interventions to prevent obesity in young women.

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Objectives: To explore reproductive outcomes in relation to occupational exposure to DDT. Methods: We inquired into the reproductive history, including total number of children, sex distribution in the offspring, time-to-pregnancy, and number of spontaneous abortions and stillbirths, of the spouses of 105 men first exposed to DDT in a 1946-1950 anti-malarial campaign in Sardinia, Italy. The time-to-pregnancy in months at the first successful conception was estimated from population Registrars. Cumulative DDT exposure during the anti-malarial campaign was retrospectively estimated. Results: The stillbirth rate was elevated and the male/female ratio in the offspring was reversed among DDT-exposed workers, and particularly among DDT applicators, compared to the unexposed subjects. Among DDT applicators, the stillbirth rate increased and the male/female ratio decreased by the tertile of cumulative DDT exposure. The fecundity ratio among spouses of DDT applicators was 0.72 (95% CI, 0.41,1.21) compared to the unexposed. The average number of children and abortion rate were unaffected by DDT exposure. Conclusions: The low statistical power of our study does not allow definitive conclusions. However, the results prompt further in-depth research into adverse reproductive outcomes and reduced fertility among men heavily exposed to DDT.


We investigated the association between total trihalomethanes (TTHMs) and risk of stillbirth and low and very low birth weight in three water regions in England, 1992-1998; associations with individual trihalomethanes (THMs) were also examined. Modeled estimates of quarterly TTHM concentrations in water zones, categorized as low (< 30 microg/L), medium (30-59 microg/L), or high (> or = 60 microg/L), were linked to approximately 1 million routine birth and stillbirth records using maternal residence at time of birth. In one region, where there was a positive socioeconomic deprivation gradient across exposure categories, there was also a positive, significant association of TTHM with risk of stillbirth and low and very low birth weight. Overall summary estimates across the three regions using a random-effects model to allow for between-
region heterogeneity in exposure effects showed small excess risks in areas with high TTHM concentrations for stillbirths \( \text{OR} = 1.11; 95\% \text{ CI}, 1.00-1.23 \), low birth weight \( \text{OR} = 1.09; 95\% \text{ CI}, 0.93-1.27 \), and very low birth weight \( \text{OR} = 1.05; 95\% \text{ CI}, 0.82-1.34 \). Among the individual THMs, chloroform showed a similar pattern of risk as TTHM, but no association was found with concentrations of bromodichloromethane or total brominated THMs. Our findings overall suggest a significant association of stillbirths with maternal residence in areas with high TTHM exposure. Further work is needed looking at cause-specific stillbirths and effects of other disinfection by-products and to help differentiate between alternative (noncausal) explanations and those that may derive from the water supply.

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Lim TL, Tan KH, Tee CS, Yeo GS.
**Investigating stillbirths using a simplified obstetric events-based protocol.**

Introduction: A stillbirth remains a distressing enigma to parents and clinicians alike as the cause often remains elusive. Few papers describe a protocol for the investigation of stillbirths. We evaluate the first obstetric events-based protocol designed for local use with an aim to adequately investigate stillbirths in a cost-effective manner. Methods: A prospective cohort study was performed on 61 stillbirths at KK Women's and Children's Hospital. There were a total of 16,980 births in the year 2000. Results: 37.7 percent of cases remained unexplained. There was protocol compliance in 51 cases (83.6 percent) with deviation in 10 cases (16.4 percent). The protocol helped to minimise costs in 18 cases (29.5 percent) as selected investigations were performed in view of obvious causes. The overall postmortem rate was 27.9 percent with the lowest rates in the Malay population. Conclusion: An obstetric events-based protocol allows clinicians to tailor their investigations easily and appropriately. It helps to provide optimal investigations and minimise unnecessary costs. It could be further fine-tuned by initiating detailed serum investigations only after delivery so as to exclude an obvious cause, like cord accidents, where full investigations are unnecessary.


Burnley H, Moore I.
**An audit to assess the quality of necropsies performed on stillborn infants.**

Aims: To determine the quality of stillbirth postmortem reports and their contribution to a final diagnosis following the introduction of explicit consent forms after the Alder Hey inquiry. Methods: Necropsy reports from 100 consecutive stillbirths were reviewed from 2001 onwards. A spreadsheet compiled data items that were considered essential in the
Royal College of Pathologists guidelines. The type of consent (with permission for organs/tissue retention) was recorded to assess the impact on establishing a cause of death. Results: Consent for tissue retention was obtained in 95 cases, whereas consent for organ retention was significantly lower (52 cases). In two cases, permission was refused for tissue retention and three requested external examinations only. Of these five, four had an undetermined cause of death, compared with 35 of 95 cases where permission for tissue retention was granted. All data items considered essential were recorded in every report. In 65 cases, the necropsy provided useful information, helped clinical care, and addressed parental concerns. Conclusions: There was no major impact of the type of necropsy consent on establishing a cause of death, apart from the case of limited necropsies without histological examination of tissue samples.

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A wave of abortions, stillbirths and deformities in sheep occurred at the Al-Ahsa oasis in the eastern region of Saudi Arabia in the second half of 1999. The abortions were recorded in August and September and stillbirths and deformities in neonates were observed in October. Adult sheep were clinically normal. A virus was isolated in chicken embryos, adapted to Vero cell culture and further identified as bluetongue (BT) virus. The virus isolated was not neutralised by the Akabane virus. Reference hyperimmune serum against antibodies to BT virus detected in the sera of the dams gave positive results for BT but negative results for both Akabane and bovine viral diarrhoea virus. It was concluded that the outbreak was caused by a virus of the BT serogroup. The authors present the clinico-pathological and epidemiological situation of the disease outbreak.


Objective: To investigate the role of intrauterine infections in unexplained second trimester abortions and stillbirths. Study Design: Histopathologic and microbiologic evidence of intrauterine infection in the placentas, fetal membranes and fetal lung tissues of 18 unexplained second trimester abortions and macerated stillbirth cases as well as the placentas and fetal membranes of 10 healthy term neonates were investigated in a Prospective Study Conducted In Ankara University School Of Medicine, Turkey. Results: Histopathologic chorioamnionitis and placental culture positivity rates in the study and control groups were 64.7 vs 0%. Bacteria were recovered from 90.9% of placentas and 36.4% of fetal lungs of the cases with histopathologic chorioamnionitis. Intrauterine infection was found in 66.7% of the whole study group, in 85.7% of the unexplained second trimester abortions, and in 54.5% of the macerated stillbirths.
Conclusion: Intrauterine infection may be an important factor in unexplained stillbirths and second trimester abortions in centers where pregnancy follow-ups lack evaluation for asymptomatic infection.

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Salihu HM, Kinniburgh BA, Aliyu MH, Kirby RS, Alexander GR.
Racial disparity in Stillbirth among singleton, twin, and triplet gestations in the United States.

Objective: We investigated the relationship between maternal race and stillbirth among singletons, twins, and triplets. Methods: We conducted a retrospective cohort study on 14,348,318 singletons, 387,419 twins, and 20,953 triplets delivered in the United States from 1995 through 1998. We compared the risk of stillbirth between pregnancies of black and those of white mothers using the generalized estimating equations framework to adjust for intracluster correlation in multiples. Results: The proportion of black infants was 16%, 18%, and 8% among singletons, twins, and triplets, respectively. Crude stillbirth rate among singletons was 6.6 per 1,000 and 3.5 per 1,000 for black and white fetuses, respectively. Among twins, 796 stillbirths (11.6 per 1,000) were recorded for black mothers versus 3,209 stillbirths (10.1 per 1,000) among white mothers, whereas among triplets there were 233 stillbirths, of which 39 stillbirths were black fetuses (24.6 per 1,000) and 194 stillbirths were white fetuses (10.0 per 1,000). Black singletons, twins, and triplets weighed 278 g, 186 g, and 216 g less than white fetuses, respectively (P <.001). Risk of stillbirth was elevated in black fetuses compared with white fetuses among singletons (adjusted odds ratio [OR] 2.9, 95% confidence interval [CI] 2.8-3.0) and twins (OR 1.3. 95% CI 1.2-1.4) but comparable among triplets (OR 1.2, 95% CI 0.7-2.1). This decreasing trend was significant (P for trend <.001). Conclusion: The disparity of stillbirths between black and white fetuses still persists among singletons and twins. Among triplet gestations, however, the 2 racial groups have a comparable risk level. Our findings highlight the need for a rigorous research agenda to elucidate causes of stillbirth across racial/ethnic entities in the United States.

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Cernach MC, Patricio FR, Galera MF, Moron AF, Brunoni D.
Evaluation of a protocol for postmortem examination of stillbirths and neonatal deaths with congenital anomalies.

A study was conducted on 75 perinatal deaths with congenital anomalies through clinical, radiographic, cytogenetic, and autopsy evaluation, and the diagnoses of 72 patients (96%) were determined. In 11 patients with chromosomal anomalies, the cytogenetic study was sufficient to determine the diagnosis and the reproductive risk. In these cases, the value of the autopsy results resided above all in the description of the clinical variability.
Radiographic evaluation was the best method to establish a diagnosis of skeletal
dysplasias (14.7%). Furthermore, the X-rays showed small skeletal defects which are
difficult to see on dissection. The clinical genetic evaluation with a detailed description of
the phenotype and anthropometric exam, performed by a clinical geneticist, and the
autopsy with gross and microscopic evaluation, facilitated the diagnoses of 50 cases
(66.7%). We concluded that, in perinatal death with congenital anomalies, the teamwork
of clinical geneticists and fetal pathologists increases the probability of determining the
etiological diagnosis. This is essential to define the parents' reproductive risk, thus
contributing to primary prevention of congenital anomalies. Copyright 2004 Society for
Pediatric Pathology

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Goldenberg RL, Kirby R, Culhane JF.
Stillbirth: A review.

Stillbirth occurs in nearly 1% of all births in the USA, and is one of the most common but
least studied adverse pregnancy outcomes. The many risk factors for and causes of
stillbirth are presented. Over the past several decades, the rate of stillbirth has been
substantially reduced, with the reduction most apparent in those stillbirths previously
occurring at term and/or in labor. Reductions have occurred because of reductions in risk
factors (i.e. prevention of Rh disease and better control of diabetes), better antepartum
monitoring of those with risk factors followed by early delivery for those fetuses found to
be at risk (i.e. growth restriction, maternal pre-eclampsia), better intrapartum fetal
monitoring, increases in Cesarean section for those at risk, and early detection of
congenital anomalies followed by termination prior to the time that these early fetal
deaths are classified as stillbirths. Finally, the value of using fetal autopsy and placental
examination to determine the cause of death accurately, both for research purposes and
for patient counseling in future pregnancies, is explored.

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Allen VM, Joseph K, Murphy KE, Magee LA, Ohlsson A.
The effect of hypertensive disorders in pregnancy on small for gestational age and
stillbirth: A population based study.

Background: Hypertensive disorders in pregnancy are leading causes of maternal, fetal
and neonatal morbidity and mortality worldwide. However, studies attempting to quantify
the effect of hypertension on adverse perinatal outcomes have been mostly conducted in
tertiary centres. This population-based study explored the frequency of hypertensive
disorders in pregnancy and the associated increase in small for gestational age (SGA) and
stillbirth. Methods: We used information on all pregnant women and births, in the
Canadian province of Nova Scotia, between 1988 and 2000. Pregnancies were excluded
if delivery occurred < 20 weeks, if birthweight was < 500 grams, if there was a high-
order multiple pregnancy (greater than twin gestation), or a major fetal anomaly. Results:
The study population included 135,466 pregnancies. Of these, 7.7% had mild pregnancy-induced hypertension (PIH), 1.3% had severe PIH, 0.2% had HELLP (hemolysis, elevated liver enzymes, low platelets), 0.02% had eclampsia, 0.6% had chronic hypertension, and 0.4% had chronic hypertension with superimposed PIH. Women with any hypertension in pregnancy were 1.6 (95% CI 1.5-1.6) times more likely to have a live birth with SGA and 1.4 (95% CI 1.1-1.8) times more likely to have a stillbirth as compared with normotensive women. Adjusted analyses showed that women with gestational hypertension without proteinuria (mild PIH) and with proteinuria (severe PIH, HELLP, or eclampsia) were more likely to have infants with SGA (RR 1.5, 95% CI 1.4-1.6 and RR 3.2, 95% CI 2.8-3.6, respectively). Women with pre-existing hypertension were also more likely to give birth to an infant with SGA (RR 2.5, 95% CI 2.2-3.0) or to have a stillbirth (RR 3.2, 95% CI 1.9-5.4). Conclusions: This large, population-based study confirms and quantifies the magnitude of the excess risk of small for gestational age and stillbirth among births to women with hypertensive disease in pregnancy.

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Fretts RC, Elkin EB, Myers ER, Heffner LJ.

Should older women have antepartum testing to prevent unexplained stillbirth?

Objective: Older women are at an increased risk for unexplained stillbirth late in pregnancy. The purpose of this study was to compare 3 strategies for the prevention of unexplained fetal death in women aged 35 years and older. We compared usual care (no antepartum testing or induction before 41 weeks), weekly testing at 37 weeks with induction after a positive test, and no testing with induction at 41 weeks. Method: We used a Markov model to quantify the risks and benefits of each strategy in terms of the number of antepartum tests, inductions, and additional cesarean deliveries per fetal death averted. Probability data used in the model were derived from obstetrical databases and the literature. Results: Without a strategy of antepartum surveillance between 37 and 41 weeks, women aged 35 years and older would experience 5.2 unexplained fetal deaths per 1,000 pregnancies. For nulliparous women 35 and older, weekly antepartum testing initiated at 37 weeks would avert 3.9 fetal deaths per 1,000 pregnancies but would require 863 antepartum tests, 71 inductions, and 14 additional cesarean deliveries per fetal death averted. A strategy of no testing but induction at 41 weeks would avert 0.9 fetal deaths per 1,000 pregnancies and require 469 inductions and 219 additional cesareans per fetal death averted. Conclusion: A strategy of antepartum testing in older women would reduce the number of unexplained stillbirths at term and would result in fewer inductions and cesareans per fetal death averted than a strategy of no antepartum testing but induction at 41 weeks.

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Ananth CV, Joseph KS, Kinzler WL.

Objective: Although twin stillbirth rates have declined substantially over the past two decades, the contribution of changes in obstetric interventions to reducing twin stillbirths has not been quantified. Methods: We carried out a retrospective cohort study of twin live births and stillbirths in the United States between 1989 and 1999 (n=1,102,212). Changes in the rate of stillbirth (> or =22 weeks) before and after adjustment for changes in labor induction, Cesarean delivery and sociodemographic factors were estimated through ecological logistic regression analysis. This analysis was based on aggregating data by each state within the United States. Results: Between 1989 and 1999, rates of labor induction and Cesarean delivery among twin live births increased by 138% (from 5.8% to 13.8%) and 15% (from 48.3% to 55.6%), respectively. These changes were accompanied by a 43% decline in the stillbirth rate between 1989 and 1999 (from 24.4 to 13.9 per 1000 fetuses at risk). After excluding births weighing < 500 g, rates of labor induction among twins at 22-27 weeks', 28-33 weeks' and > or =34 weeks' gestation increased by 95%, 131% and 127%, respectively, between 1989 and 1999. Cesarean delivery rates also increased by 55%, 29% and 2% in these same gestational age categories. The 48% (relative risk (RR) 0.52, 95% confidence interval (CI) 0.49-0.55) decline in stillbirth rate between 1989-91 and 1997-99 was reduced to a 25% (RR 0.75, 95% CI 0.72-0.79) decline after adjustment for changes in labor induction and Cesarean delivery. The decline in the rate of twin stillbirths was larger at later gestational ages (at > or =32 and > or =34 weeks) where the largest absolute increases in labor induction rates were observed. Conclusions: The use of Cesarean delivery and especially labor induction for twin pregnancies has increased substantially in the United States over the last decade and these changes have been associated with a large decline in the rate of stillbirth among twins.

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Case-control study of factors associated with intrauterine fetal deaths.

Objective: To study the characteristics of pregnancies that resulted in stillbirth and to determine which may possibly predict intrauterine fetal death (IUFD). Study Design: A total of 161 singleton pregnancies resulting in stillbirth at Nottingham City Hospital from 1991 to 1997 were compared with 499 live births randomly selected from the same period of time. The variables studied were the following: customized birth weight for gestational age, fetal sex, histopathologic cause of IUFD, maternal age, ethnic group, parity, maternal body mass index (BMI), smoking habit, and maternal blood group. Results: In 54.7% of the cases of stillbirth at our institution women presented with reduction or absence of fetal movements before the diagnosis of IUFD. Almost half of the stillbirths (48.4%) were small for gestational age (< 10th percentile) on the basis of gestational age-specific weight. The difference in customized birth weight between
stillbirths and live births was statistically significant (P <.0001). Increased maternal body mass index (BMI) was positively associated with stillbirth rate (P < .001), as was increased maternal age (P = .0012). Women with blood group O (P = .014) had an even higher stillbirth rate. There was no association between stillbirth rate and maternal ethnic group, maternal smoking, maternal Rhesus status, or fetal sex. Conclusions: This study found that almost half of stillborn babies were small for gestational age. Reduced fetal activity should be investigated thoroughly, with formal measurement of fetal growth as part of this assessment. Maternal blood group and maternal age were found to be important factors in IUFD. Smoking was not confirmed in this study to be a significant factor.

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We set out to estimate the association between smoking among pregnant women aged at least 40 years and pregnancy outcome by analyzing singleton live births in the United States between 1995 and 1997. The study group consisted of deliveries to mothers aged 40 years and older with two maternal age categories (20 to 29 and 30 to 39 years) as control. Although risks varied with maternal age, smoking was associated with a higher-than-expected risk for infant mortality in all maternal age categories. The highest rate of infant mortality associated with smoking after adjusting for confounding was among mothers aged 20 to 29 (hazard ratio [HR], 1.49; 95% confidence interval [CI], 1.28 to 1.75), while the lowest was among pregnant mothers in the 40 and above age category (HR, 1.03; 95% CI, 0.87 to 1.23). In utero fetal demise was highest among older smoking mothers (> /=40 years) and declined with decreasing age (p for trend <0.0001). In conclusion, the relationship between maternal smoking and pregnancy outcomes is modified by the age of the mother.


Background: Some causes of stillbirth may also lead to fetuses that are small for gestational age (have a low birth weight with respect to their gestational age) or are delivered preterm (before 37 weeks of gestation). It is not known whether the birth of a previous small-for-gestational-age or preterm infant increases the subsequent risk of
stillbirth. Methods: We assessed the associations between previous adverse outcomes of pregnancy and the risk of stillbirth in a nationwide Swedish study of 410,021 women who delivered first and second consecutive singleton infants between 1983 and 1997. There were 1842 and 1062 stillbirths during the first and second pregnancies, respectively. Results: As compared with women whose first infant was born at term (37 weeks of gestation or more) and was not small for gestational age, women whose first infant was born at term or preterm and was small for gestational age had an increased risk of stillbirth during their second pregnancy. The odds ratios for subsequent stillbirth, after adjustment for covariates known to be associated with an increased risk of stillbirth, were 2.1 (95 percent confidence interval, 1.6 to 2.8) among women with a first infant who was born at term and was small for gestational age, 3.4 (95 percent confidence interval, 2.1 to 5.6) among women with a first infant who was moderately (32 to 36 weeks of gestation) preterm and small for gestational age, and 5.0 (95 percent confidence interval, 2.5 to 9.8) among women with a first infant who was very (before 32 weeks of gestation) preterm and was small for gestational age. The odds ratio for subsequent stillbirth among women with a first stillborn infant was 2.5 (95 percent confidence interval, 1.4 to 4.7), as compared with women whose first infant was not stillborn. The rates of stillbirth in second pregnancies ranged from 2.4 per 1000 births among women whose first infant was born at term and was not small for gestational age to 19.0 per 1000 births among women whose first child was very preterm and was small for gestational age. Conclusions: Delivery of a previous small-for-gestational-age infant is an important predictor of the subsequent risk of stillbirth, particularly if the infant was delivered preterm.

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The aim of the study was to document the role of laboratory investigations for unexpected stillbirths at term. It was a retrospective casenote review of 75 unexpected stillbirths at term from 1995 to 1999, at the National Maternity Hospital, Dublin, Republic of Ireland. Investigations performed included blood tests, chromosomal analysis, autopsy and placental histology. Perinatal autopsy was the most informative investigation with positive findings in 49% of cases. There were positive placental findings in 37% of cases. Six of the 26 cases showed abnormal karyotyping. Of the blood tests performed, the Kleihauer-Betke test was most informative, revealing a feto-maternal haemorrhage in 8% of cases and anticardiolipin antibodies were positive in 4% of cases. FBC, TORCH and glycosylated Hb were negative in all 75 patients. Despite thorough investigations 32 of cases (43%) remained unexplained.

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Background: Previous studies suggest that high risk and low birthweight babies have better outcomes if born in hospitals with level III neonatal intensive care units. Relations between obstetric care, particularly intrapartum interventions and perinatal outcomes, are less well understood, however. Objective: To investigate effects of obstetric, paediatric, and demographic factors on rates of hospital stillbirths and neonatal mortality. Methods: Cross sectional data on all 65 maternity units in all Thames Regions, 1994-1996, covering 540 834 live births and stillbirths. Hospital level analyses investigated associations between staffing rates (consultant/junior paediatricians, consultant/junior obstetricians, midwives), facilities (consultant obstetrician/anaesthetist sessions, delivery beds, special care baby unit, neonatal intensive care unit cots, etc), interventions (vaginal births, caesarean sections, forceps, epidurals, inductions, general anaesthetic), parental data (parity, maternal age, social class, deprivation, multiple births), and birthweight standardised stillbirth rates and neonatal mortality. Results: Unifactorial analyses showed consistent negative associations between measures of obstetric intervention and stillbirth rates. Some measures of staffing, facilities, and parental data also showed significant associations. Scores for interventional, organisational, and parental variables were derived for multifactorial analysis to overcome the statistical problems caused by high intercorrelations between variables. A higher intervention score and higher number of consultant obstetricians per 1000 births were both independently and significantly associated with lower stillbirth rates. Organisational and parental factors were not significant after adjustment. Only Townsend deprivation score was significantly associated with neonatal mortality (positive correlation). Conclusions: Birthweight adjusted stillbirth rates were significantly lower in units that took a more interventionalist approach and in those with higher levels of consultant obstetric staffing. There were no apparent associations between neonatal death rates and the hospital factors measured here.

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Smith GC, Pell JP, Dobbie R.


Background: Caesarean section is associated with an increased risk of disorders of placentation in subsequent pregnancies, but effects on the rate of antepartum stillbirth are unknown. We aimed to establish whether previous caesarean delivery is associated with an increased risk of antepartum stillbirth. Methods: We linked pregnancy discharge data from the Scottish Morbidity Record (1980-98) and the Scottish Stillbirth and Infant Death Enquiry (1985-98). We estimated the relative risk of antepartum stillbirth in second pregnancies using time-to-event analyses. Findings: For 120633 singleton second births, there were 68 antepartum stillbirths in 17754 women previously delivered by caesarean section (2.39 per 10000 women per week) and 244 in 102879 women previously delivered vaginally (1.44; p<0.001). Risk of unexplained stillbirth associated with
previous caesarean delivery differed significantly with gestational age (p=0.04); the excess risk was apparent from 34 weeks (hazard ratio 2.23 [95% CI 1.48-3.36]). Risk was not attenuated by adjustment for maternal characteristics or outcome of the first pregnancy (2.74 [1.74-4.30]). The absolute risk of unexplained stillbirth at or after 39 weeks' gestation was 1.1 per 1000 women who had had a previous caesarean section and 0.5 per 1000 in those who had not. The difference was due mostly to an excess of unexplained stillbirths among women previously delivered by caesarean section.

Interpretation: Delivery by caesarean section in the first pregnancy could increase the risk of unexplained stillbirth in the second. In women with one previous caesarean delivery, the risk of unexplained antepartum stillbirth at or after 39 weeks' gestation is about double the risk of stillbirth or neonatal death from intrapartum uterine rupture.


Skeie A, Froen JF, Vege A, Stray-Pedersen B.
**Cause and risk of stillbirth in twin pregnancies: A retrospective audit.**

Background: The epidemiology of twin pregnancies complicated by stillbirth of one or both fetuses is a scarcely examined area. The risk of perinatal death in twin pregnancies is increased 2-5 times compared to singletons, and the identification of preventable risk factors becomes increasingly important as the number of multiple pregnancies is rising. We report the causes of death in twin pregnancies and their respective risk factors.

Methods: Twin pregnancies (n = 54) complicated by antepartum or intrapartum stillbirth of one or both twins (n = 68) and twin pregnancies with normal outcome (n = 103) in the counties of Oslo and Akershus, Norway, from 1986 to 1995 were included. The cases were classified and compared to the controls in multiple logistic regression analyses with regard to risk factors. results: The risk of stillbirth increased with monochorionicity, non-Western origin and assisted reproduction techniques (ART). The cases could be divided into eight different groups according to the primary diagnosis. The groups did not fit any of the existing cause-of-death classifications used on singleton stillbirths. Conclusions: The identification of monochorionic gestation should be made early in pregnancy to designate the level of risk. Assisted reproduction techniques leading to a high incidence of twins should be avoided. Health care professionals in the immigrant population should address the detrimental effects of consanguinity on reproductive outcome. We emphasize the need of a new cause-of-death classification for twin stillbirths.


Goldenberg RL, Thompson C.
**The infectious origins of stillbirth.**

Objective: Our objective was to determine the relationship between various types of perinatal infections and stillbirths. Study Design: By use of various textbooks on perinatal infections, multiple MEDLINE searches, and the reference list of all appropriate
manuscripts, the appropriate English language literature was reviewed to define the relationship between various perinatal infections and stillbirths. Results: Infection may cause stillbirth by a number of mechanisms, including direct infection, placental damage, and severe maternal illness. A large variety of organisms have been associated with stillbirth, including many bacteria, viruses, and protozoa. In developed countries, between 10% and 25% of stillbirths may be caused by an infection, whereas in developing countries, which often have much higher stillbirth rates, the contribution of infection is much greater. Ascending bacterial infection, both before and after membrane rupture, with organisms such as Escherichia coli, group B streptococci, and Ureaplasma urealyticum is usually the most common infectious cause of stillbirth. However, in areas where syphilis is very prevalent, up to half of all stillbirths may be caused by this infection alone. Malaria may be an important cause of stillbirth in women infected for the first time in pregnancy. The two most important viral causes of stillbirth are parvovirus and Coxsackie virus, although a number of other viral infections appear to be causal. Toxoplasma gondii, leptospirosis, Listeria monocytogenes, and the organisms that cause leptospirosis, Q fever, and Lyme disease have all been implicated as etiologic for stillbirth. Conclusion: Because infection-related stillbirth is relatively rare in developed countries, and those that do occur are caused by a wide variety of organisms, reducing this etiologic component of stillbirth much further will be difficult. However, in certain developing countries, the stillbirth rate is so high and the infection-related component so great that achieving a substantial reduction in stillbirth should be possible simply by reducing maternal infections.


Wood SL, Jick H, Sauve R.

The risk of stillbirth in pregnancies before and after the onset of diabetes.

Aims: There is significant controversy as to whether or not stillbirth is increased in pregnancies prior to the onset of diabetes. An observed increase may be indicative of risks associated with untreated gestational diabetes. It is generally accepted that the risk of stillbirth in pregnancies that occur after the onset of diabetes has been diminished by modern obstetric care. However, the degree of residual risk is not well quantified. This study sought to examine the rates of stillbirth before and after the onset of diabetes compared with the general population. Methods: Retrospective cohort and nested case-control study. The study population was drawn from the UK-based General Practice Research Database, comprising some 300 practices, with data collection from the late 1980s until September 1999. From the base population, 913 diabetic women who had had a pregnancy were identified and 10,000 subjects without diabetes were randomly chosen as controls. Stillbirth was defined as death in utero after 20 weeks or with birth weight >500 g. Results: The stillbirth rates were higher in prediabetic pregnancies (19.7/1000), and in those occurring after the diagnosis of diabetes (33.7/1000), compared with the non-diabetic population (5.5/1000). Stillbirths were matched to four live births by maternal age and year of birth. Prediabetic pregnancy and pregnancy after the onset of diabetes were strongly associated with stillbirth: odds ratio (OR)=4.68 (1.67, 13.08) and
OR=4.39 (2.22, 8.64), respectively. Conclusions: The risk of stillbirth was increased in both prediabetic and post-diabetic pregnancy.


Lauenborg J, Mathiesen E, Ovesen P, Westergaard JG, Ekbom P, Molsted-Pedersen L, Damm P.

Audit on stillbirths in women with pregestational type 1 diabetes.

Objective: To audit stillbirth cases in women with type 1 diabetes to search for specific characteristics in order to improve antenatal care and treatment. Research Design And Methods: Retrospectively identified cases of stillbirths in women with type 1 diabetes during 1990-2000 were analyzed regarding characteristics of the mother, the pregnancy, glycemic control, and the stillborn. The cause of stillbirth was categorized as explainable, likely, or without obvious cause. Results: We found 22 women with 25 stillbirths among 1,361 singleton births by women with type 1 diabetes. In seven stillbirths the cause was categorized as explainable and in six as likely. In 12 cases no obvious cause was found; however, glycemic control was suboptimal in 9 of these cases. A total of 14 women reported daily smoking, and 10 of 19 with low education were unemployed. Conclusions: Women experiencing stillbirth were characterized by a high incidence of suboptimal glycemic control, diabetic nephropathy, smoking, and low social status.

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de la Vega A, Verdiales M.

Failure of intensive fetal monitoring and ultrasound in reducing the stillbirth rate.

Although highly popularized among obstetricians, there are conflicting results regarding the efficacy of high-resolution ultrasound and other fetal well-being tests on improving neonatal outcome and morbidity. To assess the impact of unrestricted fetal well-being tests and sonographic evaluations on the stillbirth rate, we evaluated a total of 1,810 pregnancies 20 weeks of gestation or more from a single private clinic serving a mixed population of high and low-risk patients. All patients were performed high-resolution sonography during each trimester of pregnancy. In addition, on each prenatal visit, fetal heart rate, position and amniotic fluid index were documented by a limited sonographic scan. Further sonographic studies were done whenever deemed necessary depending on the clinical situation. Biophysical profiles were performed in the third trimester at any time a risk factor was identified, and repeated as frequently as estimated necessary. All cases of fetal death in utero were documented and the associated maternal risk factors assessed. A total of 14 stillbirths occurred among the 1,810 patients. The stillbirth rate for this population was determined to be 7.7/1000 births (U.S. national average of 6.7-7.8/1000 births). The most common associated maternal complications were Diabetes (4 cases) and Antiphospholipid syndrome (3 cases). All except for one fetus lost at 37 weeks
had at least one identifiable maternal risk factor. These results prove that intensive fetal surveillance, even when unrestricted by economic concerns, has limited effectiveness in avoiding fetal demise. This is most probably due to acute placental and cord accidents that cannot be detected promptly enough or that are simply unavoidable.

Matturri L, Minoli I, Lavezzi AM, Cappellini A, Ramos S, Rossi L. 
**Hypoplasia of medullary arcuate nucleus in unexpected late fetal death (stillborn infants): A pathologic study.**

Objectives: To evaluate the frequency, morphology, and pathogenesis (primary or secondary) of the abnormally developed medullary arcuate nucleus (ARCn) in stillbirths. Methods: We examined 26 stillbirths (24 antepartum, 2 intrapartum) that had a gestational age between 25 and 40 weeks and a normal karyotype. All of the stillborns were described as well-developed, with body length and weight proportional to their gestational age. Each case was submitted to complete autopsy examination, which included a systematic gross and microscopic evaluation of the body, the placental disk, and the umbilical cord and membranes. The brainstem was the particular focus of the histologic examination. The study of the various nuclei (nucleus hypoglossus, dorsal vagus motor nucleus, tractus solitarii nucleus, nucleus ambiguus, trigeminal tractus and nucleus, arcuate nucleus, and ventrolateral reticular formation and its neurons and parabrachial/Kolliker-Fuse complex) was performed on transversal serial sections through the entire pons and medulla oblongata. The histologic analysis was supplemented by volumetric reconstruction and immunohistochemical detection of both apoptosis and proliferating cell nuclear antigen. Results: Histologic examination showed abnormalities of the medulla oblongata ARCn in 9 fetuses (35%). In 8, a marked hypoplasia was evident, characterized by a volume reduction of the nucleus accompanied by neuronal depletion, whereas in 1 fetus the nucleus was completely absent (agenesis). The absence of gliosis, the negativity of the proliferating cell nuclear antigen analysis, and the similarities in apoptotic indices between the hypoplastic and well-developed arcuate are in keeping with a primary developmental defect. This anomaly is frequently associated with hypoplasia of the reticular formation and chronic hypoxia. Conclusions: A high frequency of hypoplasia of the ARCn occurs in fetuses who have died "sine causa," ie, in a similar manner to that observed in sudden infant death syndrome. Chemoreceptors, although not involved in reflexogenic oxygenation in fetal life, become of vital importance intrapartum and postpartum; therefore, whenever impaired in the course of development, chemoreceptors may underlie cardioventilatory abnormalities critical to sudden infant death syndrome


Bartellas E, Van Aerde J. 
**Bereavement support for women and their families after stillbirth.**
Objectives: (1) To heighten awareness of the grieving process of the mother and her family experiencing the death of a baby; (2) to offer suggestions to health-care providers of the type of support that will achieve optimal grief resolution. Options: Early, late, or no interventions for women and families who experienced stillbirths. Outcome: Success of health-care providers in preventing, recognizing, and treating psychological problems in the bereaved parents and families, and also in helping these families to build meaningful experiences and positive memories from their loss. Evidence: English-language articles and their references on grief and bereavement after perinatal death, through a search of MEDLINE, the Cochrane Library, and publications of other national bodies including the Canadian Paediatric Society, and the American College of Obstetricians and Gynecologists.


Neuropathologic findings in stillbirths oftentimes provide insight into the specific mechanisms leading to death. Examination of the brains of stillborn infants may also identify pathophysiologic processes that result in prenatal brain injury in liveborn as well as stillborn infants and that lead to neurologic disorders in liveborn infants, such as cerebral palsy or the sudden infant death syndrome (SIDS). A variety of abnormalities are found in the brains of stillborns, the most common including cerebral white matter necrosis (periventricular leukomalacia) or gliosis, germinal matrix or intraventricular hemorrhage, cerebral infarcts, pontosubicular necrosis, and spinal cord or brainstem necrosis. The 2 major hypotheses that have been proposed for the pathophysiology of cerebral white matter injury in the perinatal period are hypoxia/ischemia and infection/cytokines as the basis for injury. The fetal brain may be selectively vulnerable to various insults at specific stages of development.

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This article reviews the literature on infectious diseases as a cause of stillbirth. Identifying a specific infection as a cause of stillbirth is limited by many obstacles. Nevertheless, "good faith" efforts estimate that approximately 9% to 15% of stillbirths are caused by infections. Infection may be especially important as a cause of stillbirth occurring early in pregnancy. Recognized causes include syphilis, toxoplasmosis, parvovirus B-19, chorioamnionitis, and Listeria monocytogenes. Other organisms that are "purported to cause" stillbirth include the genital mycoplasmas, Chlamydia trachomatis, HIV, group B streptococci, and others. No single strategy has been developed for effective prevention of stillbirth caused by infection. Six potential strategies and their rationale are presented, but the low rate of stillbirth in most situations would require large intervention trials for hypothesis testing. Infection is an important cause of stillbirth.
Within the framework if determining epidemiological etiology, research should be initiated in the role of infectious causes.

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The authors evaluated the association between alcohol intake during pregnancy and risk of stillbirth and infant death in a cohort of pregnant women receiving routine antenatal care at Aarhus University Hospital (Aarhus, Denmark) between 1989 and 1996. Prospective information on alcohol intake, other lifestyle factors, maternal characteristics, and obstetric risk factors was obtained from self-administered questionnaires and hospital files, and 24,768 singleton pregnancies were included in the analyses (116 stillbirths, 119 infant deaths). The risk ratio for stillbirth among women who consumed > or =5 drinks/week during pregnancy was 2.96 (95% confidence interval: 1.37, 6.41) as compared with women who consumed <1 drink/week. Adjustment for smoking habits, caffeine intake, age, prepregnancy body mass index, marital status, occupational status, education, parity, and sex of the child did not change the conclusions, nor did restriction of the highest intake group to women who consumed 5-14 drinks/week (risk ratio = 3.13, 95% confidence interval: 1.45, 6.77). The rate of stillbirth due to fetoplacental dysfunction increased across alcohol categories, from 1.37 per 1,000 births for women consuming <1 drink/week to 8.83 per 1,000 births for women consuming > or = 5 drinks/week. The increased risk could not be attributed to the effect of alcohol on the risk of low birth weight, preterm delivery, or malformations. There was little if any association between alcohol intake and infant death.