

Compilation of Stillbirth Research Abstracts Presented at the 2006 Conference in Japan

Epidemiology of Stillbirth in Japan

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Japan has become a country with the lowest perinatal mortality rate in all over the world. However, the low but significant still birth cases are still present. Despite, even in Japan, social, medical, economical and many other factors are apparently related with the cause of stillbirth, not only general Japanese but obstetricians are likely to escape discussions for the present status and the remnant duty for preventing unnecessary abortion or psychological trauma to mothers. Herein, I report the present epidemiological status and chronological change of stillbirth in Japan, based on Perinatal Registration Database by Japanese Society of Obstetrics and Gynecology, and discuss the presence and future in stillbirth in Japan.

Chronological Changes of Perinatal Vital Statistics in Japan

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The perinatal mortality rate was analyzed using Japanese vital statistics. For Japan as a whole, it is possible to compile a satisfactory series of vital statistics since 1900. The perinatal mortality rate significantly decreased with the year. Although the perinatal mortality rate fell by 70% between 1980 and 2000, it does not change for recent several years. Changes in the distribution of birthweight, maternal age, and plurality are thought to attenuate the observed reduction in perinatal mortality. In order to decrease perinatal mortality rate further it is necessary to improve the organization and quality of perinatal care.

Outcome of Fetal Anomalies Prenatally Diagnosed Early in Gestation

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Termination of pregnancy prior to 22 weeks gestation is legally permitted in present Japan. Since prenatal screening test was introduced in many hospitals, many cases with fetal anomalies have been diagnosed early in gestation.

Our center is one of the biggest tertiary center with maternal-fetal unit in Japan and about 700 cases have been prenatally diagnosed since our center established in 2002. Outcome of fetal anomalies prenatally diagnosed prior to 22 weeks gestation in our center was studied in this study. Many of the cases resulted in termination of pregnancy. Some of the cases were estimated good

prognosis after birth. We discuss ethical issues of the fetal diagnosis early in gestation in Japan.

Towards an International Classification of Stillbirth

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Clinical audit is becoming an established and essential component of modern care. International agencies including WHO, UNICEF and FIGO are helping to spread good practice and recognize perinatal audit as an important driver for ensuring that maternal and perinatal services receive appropriate local recognition and resources.

Stillbirth is the most common cause of perinatal loss, and a source of intense grief for the mother and family. Yet it is under-reported in many countries, and there has been little advance in understanding the causes. Reasons for this may include a lack of training, resources for data collection, and availability of pathological services. But even in countries such as the United Kingdom with its strong history of audit including confidential enquiries, progress has been slow; in fact national stillbirth rates have seen a sustained rise over the last three years. It has finally being recognised that the current classification system, which results in the majority of cases being reported as 'unexplained', is not helpful in any attempts to develop a strategy for prevention.

A good classification system for still birth is important at several levels - for the parents, clinicians, and the health service in general. A number of new methods have sprung up around the world, which each seek to improve the understanding of what has gone wrong, and the processes which have led to the loss. The challenge now is to synthesise what can be learnt from these efforts, and to standardise the definitions as well as the classification systems so that comparisons can be made between different centres and countries. This will help to benchmark clinical performance, to prioritise services, and to foster international collaboration and research.

Current Classifications Systems for Stillbirth

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Background Stillbirths first became notifiable in Scotland in 1940, and perhaps the earliest classification aimed at audit and surveillance was that of Sir Dugald Baird and his colleagues in Aberdeen¹. Since then, classification systems for perinatal deaths have flourished. But what do they tell us? What makes a "good" classification system?

Aims To undertake a systematic review of current classifications of stillbirth and to evaluate the classifications in terms of: usefulness; conservation of available relevant clinical and pathological information; ability to expand into sub-classifications; clarity of instructions and definitions for use; and reproducibility.

Methods All publications which described the causes of stillbirth after 1994 were eligible for inclusion. A comprehensive literature search was undertaken which included electronic databases (Medline, Cochrane Library 1995-2005) and websites of key professional organisations. The search was conned to the English language. Identified reports were cross referenced and experts in the field were contacted. In the case of duplicate publication (the same classification system), the most recent and comprehensive publication was chosen for inclusion. Classifications were rated and compared.

Results The results will be presented.

References

1. Baird D, Wyper JFB. High stillbirth and neonatal mortalities. Lancet 1941;ii, 657-9.

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Integrating the Purposes of Stillbirth Classifications

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A variety of classifications of stillbirths exist, and new ones continue to be proposed, as none cover all the needs experienced by the Users. Classifications are often created specifically for an observed need in epidemiology, clinical care, pathology, or basic science -; but unfortunately never useful for all. Some crave simplicity, others detail. These different points of view entail differences in e.g. whether a classification classify causes of death, or causes and associated conditions alike, whether there is a hierarchy in what category is of the highest importance, or all categories being of equal significance, and whether antepartum deaths are distinguished from intrapartum or not.

Ideally, a classification must accurately categorize stillbirths in a way that is equally useful for three purposes:

- 1) Provide epidemiology of what preventable and non-preventable pathologies and conditions constitute the major threats to healthy pregnancies in any given population-;; in developed as well as in developing regions.
- 2) Provide information for the clinician in counseling the affected couple on future risks and options available for her health and reproduction.
- 3) Provide defined and detailed entities of pathologies to enable research to improve understanding, prevention and treatment of lethal pathologies in pregnancy.

These three goals may seem to compete, representing different levels of detail needed and wanted. However, these three 'levels' of information reflect the various practical situations in developing versus developed communities, their access to specialized perinatal care and pathology services, and their commitment to and resources for research. The first basic level should reflect the needs for international comparisons and be useful in any community. The second specific level should reflect the clinical needs in communities with specialized perinatal care available. The third complete level should fulfill the needs of research and communities aiming at optimal care. For an "all-purpose" classification, it must be expandable in both depth and detail, and easily retrievable in different forms, it must accommodate as much information on both cause of death as well as events and associated conditions of clinical relevance, and should also enable the identification of lacking information as opposed to pathologies and deaths caused by mechanisms that remain unidentifiable by current knowledge.

We propose a classification of fetal causes of death & associated conditions (CODAC), consisting of main categories of lethal events and conditions, supplemented by up to two clinically relevant associated conditions. We report its performance and ability of cross-coding to existing classifications.

Registration and Reporting Births and Stillbirths at Borderline Viability - Effect on Perinatal and Infant Mortality Rates

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Purpose To determine the variability in interpretation of definitions of live birth and stillbirth for babies born at the edge of viability and the potential impact on perinatal and infant mortality rates.

Method Provincial vital statistics registrars, physicians attending a national conference, and selected physicians from three provinces were asked to indicate if a birth event described in several case scenarios would be registered with vital statistics as a live birth or stillbirth based on their interpretation of vital statistics definitions.

Results There was great variability in the interpretation of definitions of birth and stillbirth for certain birth events and confusion between requirements for registration and the reporting of these birth events for comparative purposes. This is likely due to the discrepancy amongst WHO definitions, requirements of Vital Statistics Acts, ICD-10 coding standards and physician recording practices. The inclusion or exclusion of births at borderline viability could have important effects for national or international comparisons of data.

Discussion There is significant variability in interpretation of definitions of livebirth and stillbirth that could adversely effect reported mortality rates.

Implications The Canadian Perinatal Surveillance System has established a group to work towards developing national standards and guidelines to promote consistency in recording of livebirths and stillbirths at borderline viability. The opportunity to present and discuss this issue at an international conference will be an important component to the consultation process.

Unexplained Cause of Intrauterine Fetal Death using Different Classification Systems

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Aim A consistent system for the classification of intrauterine fetal death (IUF D) is essential for evaluating quality of care, proper statistics and development of preventive strategies. Different classification systems exist. Unfortunately in 20-50% of cases the cause of IUF D remains unknown. Our objective was to investigate whether the group with unknown cause of death varies across classification systems.

Methods Our panel of 2 obstetricians, a perinatal pathologist, a registrar and a data manager classified singleton pregnancies > 20 weeks of gestation for which the diagnosis of IUF D was determined before labour. These IUF D's occurred in 54 centres participating in our national multicenter cohort study during a 3 year period (2002-2005). Classification systems used were the widely used Extended VVigglesworth and the Modified Aberdeen classification systems and the new Tulip classification.

Results Inventarisation of 325 cases resulted in 288 cases (89%) classified as unexplained ante partum fetal death or unclassifiable in the extended VVigglesworth classification. In the Modified Aberdeen 197 cases (61%) were classified as unexplained or unclassifiable and in the Tulip classification 82 cases (25%) were classified as unknown; despite thorough investigation or unknown; important information missing. 208 (72%) of the 288 cases with unknown cause in the VVigglesworth classification received a known cause of death in the Tulip classification. Placental bed-pathology was allocated in 119 cases, placental pathology; development in 33 cases, placental pathology parenchyme in 11 cases, umbilical cord complication in 20 cases, placenta not otherwise specified in 18 cases, Fetal hydrops of unknown origin in 2 cases, Maternal disease; diabetes mellitus in 1 case and Maternal disease; other in 4 cases.

Conclusion From one cohort the percentage of IUF D's with unknown cause of death varies across classification systems. The Tulip classification gives more insight into the cause of IUF D than the VVigglesworth and the Aberdeen classification. This is partly due to the fact that the VVigglesworth and the Aberdeen were not specially designed for IUF D.

Classification of the Causes of Fetal Death in Multiple and Singleton Pregnancies

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Aim: To identify the main causes of fetal death in multiple pregnancies and to compare these with singleton causes using the PSANZ Perinatal Death Classification (PSANZ-PD C) system. **Methods:** Three states (Queensland, Victoria, and Western Australia) contributed to this analysis. Two states contributed data on all fetal deaths over the four-year period 2000-2003 and one state contributed data from the two-year period 2002-2003. Fetal deaths of 20 weeks or more gestation registered within each state & # 352;s perinatal data collection were included. All deaths were classified through the respective Health Departments using the PSANZ-PDC. Each state electronically submitted nonidentifiable aggregate data to the coordinating centre for analysis. The main causes of fetal death in multiple pregnancies were compared with singleton pregnancies. Subgroup analyses were performed according to gestational age. **Results:** A total of 499 389 births were included. The overall fetal death rate (FDR) was 7.1/1000 births. A total of 350 fetal deaths of multiple pregnancies and 3180 singletons were included in the analysis. The FDR for singletons was 6.6/1000 and 21.2 for multiples. The four leading categories of fetal death for multiples (contributing 84% to the total) were: Specific prenatal conditions (mainly twin-twin transfusion) (35.4%); Spontaneous preterm (23.7%); Unexplained antepartum death (14.6%); and Congenital abnormality (10.9%). The main categories for singletons (contributing 72%) were: Unexplained antepartum death (28.2%); Congenital abnormality (20.4%); Maternal conditions (12.8%); Spontaneous preterm (10.2%). The categories with the highest relative risk for multiples when compared with singletons were: Specific perinatal conditions; Spontaneous preterm; No obstetric antecedent; and Hypertension. **Conclusions:** This analysis which included data from three Australian states highlights differences in causes of fetal death for multiple pregnancies. The contribution to fetal death in multiple pregnancies from spontaneous preterm birth and twin-twin transfusion overwhelmed all other categories, whereas for singleton pregnancies, longer gestation allowed unexplained fetal death to be the dominant category. Nevertheless, it should be noted that the rates of fetal death are higher for multiple pregnancies in virtually every category. More systematic reporting of chorionicity in central perinatal databases will enable more meaningful analyses of the causes of fetal death in multiple pregnancies.

Stillbirth Investigation Protocols : A Systematic Review

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Objectives This systematic review was conducted to support the Alberta Medical Association Committee on Reproductive Care in its effort to update their stillbirth investigation protocol against the evidence for best practice. The Alberta Perinatal database reports a stillbirth rate of 6.5 per 1000 with a autopsy rate of 54%. This review aims to identify the most appropriate components of a protocol for determining the cause(s) of stillbirth and to identify protocols recommended by professionals worldwide.

Methodology A systematic search of the medical literature published between 1985 and June 2005 was conducted to identify primary research studies and publicly available formal protocols. The search included Cochrane Library, PubMed, EMBASE, CINAHL, HealthSTAR, Science Citation Index, BIOSIS. The methodological quality of the included research studies was assessed according to specific criteria.

Results Currently there is no generally accepted reference protocol for stillbirth investigation. Five publicly available formal protocols, which were selected for this review, recommend extensive and comprehensive stillbirth investigation, outlining similar steps. Although these protocols differ in many of their recommendations, they agree on including several elements for routine investigation. For example, they all recommend a complete autopsy, performed in a skilled and timely manner (even if the cause of death appears evident), and detailed cord and placenta examinations. Evidence on the value of specific components of stillbirth investigation was poor with limited reporting of data. Only general conclusions could be drawn from the 7 research studies that met the inclusion criteria. They showed that there is value in routinely performing fetal autopsy and placental examinations as integral components of a stillbirth investigation. It is not clear which other components should be included in a stillbirth investigation protocol.

Conclusions No firm scientific judgment could be made on which is the most appropriate stillbirth investigation protocol. There is no generally accepted reference protocol for stillbirth investigation. It is yet to be determined which components should be considered the most relevant and efficient for stillbirth investigation. Findings from this review highlight the value of fetal autopsy and placental examination, which remain important in the confirmation and further delineation of the cause of fetal death, assuming a high quality of the postmortem examination. This information may be helpful in counseling patients who are considering whether or not to consent to a postmortem examination following a stillbirth.

Pathological Assessment of Fetal Death

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Background: When a stillbirth occurs, every effort should be made to determine the cause of the fetal death because of correct diagnosis and future pregnancy as well as mental health of the family. The postmortem examination is essential to detect the causes of the fetal death. The aim of this study is to estimate the value and quality of the postmortem examination.

Method: We examined 234 autopsy les of stillbirths at Osaka Medical Center and Research Institute for Maternal and Child Health during five years between 1996 and 2000, retrospectively. We performed autopsy, placental examination, total body X ray examination and chromosome analysis if possible as the postmortem examination.

Results: We could determine the true causes of fetal death in 203 cases (87%) pathologically. There were various causes of fetal death including 39 placental abnormalities (amniotic band syndrome; 10), 36 multiple births (TTTS; 21), 22 chromosome aberrations (18 trisomy; 5), 20 central nerve system abnormalities (anencephaly; 6), 18 renal diseases (Potter sequence); 6), 13 cystic hygromas without chromosome aberrations, 12 bone dysplasia (osteogenesis imperfecta; 5), 12 body wall abnormalities (prune belly syndrome; 3) and 7 congenital heart diseases. 149 cases were in agreement with clinical diagnoses and we could have more information in detail on 67 cases after placental, chromosomal and total body X ray examinations. 15 cases were inconsistent diagnoses in which the cases of amniotic band syndrome were the most frequent. 45 (64%) of 70 cases could be clarified pathologically which were diagnosed as intrauterine death due to unknown etiology clinically.

Conclusion: 87% cases of stillbirths and 64% cases of intrauterine death due to unknown etiology revealed the true causes of fetal death. The postmortem examination should be performed in terms of correct diagnosis and future pregnancy. It is important to examine not only fetuses but also placental, chromosomal and total body X-ray examinations to determine the cause of fetal death perfectly.

Medical Management of Lethal Malformed Fetuses Diagnosed in Utero

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The cases which are prenatally diagnosed fetal malformations are increasing along with the prevalence of antenatal ultrasonography in Japan. Some of them are complicated with lethal/incurable malformations. The perinatal death after 22 weeks gestation occurs in 6-9 % in our institute which is a tertiary perinatal care referral center. The most of the cases with malformed fetuses referred to our institute are already over 22 weeks gestation which is the limit for termination permitted by Japanese law. When the malformed fetuses are diagnosed as lethal/incurable, it is necessary to do careful maternal medical care with the respects of fetal life. Sometimes it is hard to make accurate diagnosis of the fetus, but it is important to inform the couple about the fetal status with sensible consideration.

The discussion of the timing and the mode of delivery to avoid maternal complications should be followed after the information of the fetal status. Although delivery by cesarean section is ultimately the parents' decision, our recommendation is to avoid invasive procedures involving both the mother and infant based on fetal indication alone. Obstetricians, neonatologists, medical geneticists, nurses, midwives and medical social workers are involved in this discussion. If a decision has been made by the couple to avoid invasive procedures, the infant is delivered and we provide care for the infant making him/her as comfortable as possible. After the diagnosis made, the grief care should be start in the cooperation with medical team. It should be avoided to let the couple to feel like the fetus/infant is ignored because of the lethal/incurable condition. We should not forget the respectful attitude for the fetus/infant. Also, it is an important work to clarify the cause of malformations including physical examination, genetic examination, and autopsy of the fetus/infant, and it is necessary to evaluate the risk of recurrence in the future pregnancy. They would play great roles in grief work of the couple.

Postmortem and Placental Lesions in Term Stillbirth

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Learning Objectives

1. Review the techniques of standardized postmortem and placental examination
 2. Review the postmortem and placental lesions associated with term stillbirth
- Abstract /Summary Between 1994-2005, we examined 737 stillbirth and their placentas at Women and Infants Hospital, Brown Medical School. There were 158 (21%) term cases. 97 (61%) cases showed findings consistent with established cause/strong association with stillbirth such as amniotic fluid infection syndrome, placental abruption, fetal vascular compromise, twin-twin transfusion syndrome, maternal fetal hemorrhage, multiple congenital malformations with/without aneuploidy. In 61 cases (38%), no established cause or association to explain demise could be identified. Placental findings in this group mostly comprised of cord lesions, abruptio placenta and changes consistent with maternal diabetes and thrombophilic states.

Cause of Intrauterine Fetal Death. Value of Autopsy and Placental Examination to determine a Placental Cause

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Aim More insight into cause of intra uterine fetal death (IUFD) is needed as this remains unknown in 20-50% of cases. Minimal information about value of diagnostic tests after IUFD in order to find the cause of death is available. No international evidence-based fetal guidelines for use of diagnostics after IUFD

exist. Value of autopsy and placental examination seems promising. Our objective was to investigate cause of IUD and determine the value of autopsy and placental examination in our largest death group.

Methods Our panel of 2 obstetricians, a perinatal pathologist, a registrar and a data manager classified singleton pregnancies >20 weeks of gestation for which diagnosis of IUD was determined before labour. These IUD's occurred in 54 centres participating in our national multicenter cohort study during 2002 to 2005. The Tulip classification was used. Cause of death was defined as that pathophysiological entity which was responsible for the irreversible path to death. Diagnostics were valued as not contributing, confirming, excluding or missing.

Results A total of 325 cases of IUD were evaluated. 20 cases (6.2%) were classified in the group Congenital Anomaly, 204 (62.7%) in Placenta, 5 cases (1.5%) in Fetal Infection, 8 cases (2.5%) in Fetal hydrops unknown origin. 6 cases (1.8%) in Maternal disease and 82 cases (25.2%) in Unknown. Value of autopsy and placenta in the different placenta cause of death groups was not contributing, confirming, excluding or missing. For the placental bed pathology group for autopsy this was respectively: 44, 3, 55 and 18, for placenta this was: 7, 111, 1 and 1. For the subgroup placental pathology development for autopsy: 11, 3, 15 and 5 and for placenta: none, 34, none and none. For the placental pathology group parenchyme for autopsy: 5, 1, 6 and none and for placenta: 1, 10, 1 and none. For the umbilical cord complication group for autopsy: 10, 4, 3 and 3 and for placenta: 1, 14, 5 and none. For the group placenta not otherwise specified for autopsy: 7, none, 6 and 5 and for placenta none, 18, none and none. In 96 cases (47.1%) autopsy and in 194 (95%) cases placental examination was either confirming or excluding.

Conclusion Largest death group in our IUD cohort was Placenta. In almost all cases placental examination was valuable; autopsy in half of cases. Placental examination as diagnostic test after IUD should always be done. Autopsy can give useful information.

Maternal Stress and Preterm Birth: The Intrauterine Paradigm

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There is a growing body of empirically sound research that suggests pregnant women of different racial, ethnic, socioeconomic, and national backgrounds who experience high levels of psychosocial stress during pregnancy are at significant risk for shorter gestation and earlier onset of spontaneous labor and preterm delivery. Another considerable literature supports the notion that inflammation is associated with preterm birth and that stress and inflammation are linked together in the etiology of preterm birth. Stress and inflammation are mutually synergistic, i.e. inflammation produces cytokines (interleukin (IL)-1, IL-6, IL-8, tumor necrosis factor (TNF)-), some of which amplify stress, and stress produces hormonal (corticotrophin releasing hormone (CRH), cortisol, prolactin) changes that regulate cytokine production. These systemic hormonal/cytokine

mediators of stress activate the intrauterine tissues, decidua, placenta and myometrium, invoking physiological changes that cause preterm birth. Uterine activation refers to increased expression of the genes and their proteins (uterine activation proteins, UAPs) that promote the ability of the uterine tissues to carry out the processes of parturition, often as intermediates in feed-forward mechanisms as we will illustrate.

These UAPs include the oxytocin receptor (OTR), prostaglandin (PG) endoperoxide H synthase (PGHS-2), the PGF₂ receptor, FP, connexin-43 (CX-43), the matrix metalloproteinases (MMPs), or decreased tissue inhibitor of metalloproteinases (TIMP-1) and inducible nitric oxide synthase (iNOS). We will discuss a unifying hypothesis that ties together stress mediators and UAPs in a model of maternal tissues that attempts to explain how maternal stress causes preterm birth. Recent work will be described that suggests two proteins induced by cytokines, the enzyme 11 β -hydroxysteroid dehydrogenase type 2 (11 HSD2) and FP, may be key linking steps between stress mediators and uterine activation. This construct will incorporate elevated levels of stress mediators (hormones and cytokines) which alter enzymatic systems (e.g. placental and decidual 11 β -HSD2, PGHS-2, MMPs, TIMP-1, or iNOS) and receptors (FP, OTR) that further amplify both the stress mediator levels and the UAPs in maternal intrauterine tissues, consequently leading to preterm birth.

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First Trimester Determination of Adverse Pregnancy Outcome.

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The timing of factors which lead to disorders of fetal growth have been studied for many years. Previous studies have focused on disorders of the "second wave" of trophoblast invasion of myometrial arterioles and on fetal weight gain in the third trimester. Over the last five to ten years, clinical studies have demonstrated associations between first trimester ultrasound and biochemical parameters and the risk of later adverse perinatal outcome. First trimester growth restriction is associated with an increased risk of low birth weight, low birth weight percentile for gestational age and extremely preterm birth. This may reflect a defect in early pregnancy placentation and later adverse outcome. Consistent with this hypothesis, low first trimester circulating maternal concentrations of pregnancy associated plasma protein A (PAPP-A), a trophoblast-derived regulator of the insulin-like growth factor system, are associated with an increased risk of later stillbirth, growth restriction, preterm birth and pre-eclampsia. Even among healthy women having normal pregnancies, first trimester circulating concentrations of PAPP-A correlate with the timing of spontaneous labor and the eventual birth weight. In the case of stillbirth related to placentally-related complications (abruption and growth restriction), women with low maternal

serum levels of PAPP-A in the first 10 weeks post-conception have a relative risk of stillbirth in late pregnancy in the region of 40-50. Two caveats apply to this observation. first, the high relative risk reflects an extremely low risk of such events in women with normal or high values of PAPP-A. Second, the study was relatively small scale and larger scale studies are required to characterize fully this association. Nevertheless, these analyses suggest that in some women complications of late pregnancy have their origins in the very earliest weeks of gestation and precede first attendance for prenatal care. These findings have implications for strategies aimed at detecting women at increased risk of stillbirth.

Placental Etiologies of Fetal Growth Restriction and Stillbirth

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Learning Objectives

1. Review of current knowledge in placental growth
2. Review placental conditions that are associated with growth restriction and stillbirth

Abstract /Summary

The placenta is a unique organ which forms during gestation and loses its utility after parturition. Although hosted by the mother and supports the fetus, it originates from the embryo thus of fetal origin. The interface of maternal tissues and the developing placenta is complex. Recent developments describing some of the basic molecular pathways have contributed significantly to our understanding of normal placental growth. Between 1994-2005, we examined 737 stillbirth and their placentas at Women and Infants Hospital, Brown Medical School. There were 471 cases that showed findings consistent with established cause/strong association with stillbirth such as amniotic fluid infection syndrome, placental abruption, fetal vascular compromise, twin-twin transfusion syndrome, maternal fetal hemorrhage, multiple congenital malformations with/without aneuploidy. 266 cases did not show an established cause or association with stillbirth .

When growth restriction was analyzed as an independent variable, 28% (131) of the 471 cases had impaired fetal and/or placental growth. In contrast, 58% (158) of the cases in the undetermined group were growth restricted. Placental findings in this group included abnormalities of placental shape, lesions that might compromise fetal circulation such as abnormal umbilical cord insertions, villous remodeling abnormalities, abnormal vasculogenesis and impaired trophoblast turnover.

Suboptimal Growth and the Risk of Stillbirth

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Stillbirth is one end of a spectrum of conditions associated with fetal growth restriction, which also include increased risk of spontaneous and iatrogenic

preterm birth, perinatal morbidity, neonatal mortality, sudden infant death, cerebral palsy and delayed effects into adult life. Fetal growth restriction should trigger referral for further investigation but is in most instances not recognised as such antenatally. Retrospective definition of growth restriction requires an adjustment or customization of the birthweight standard for physiological variables such as maternal height, weight in early pregnancy, parity, ethnic origin, and the sex of the baby. This results in a sharper distinction between constitutional and pathological smallness. Using this method, we studied a database of 2625 stillbirths (24+ weeks gestation) which occurred in the West Midlands between 1997-2003, representing an average rate of 5.8/1000 [1]. A total of 1371 (52%) of all stillbirths were below the 10th customized percentile, but 242 of these could be assigned other conditions such as congenital anomaly and infection, leaving a total of 43% with a primary diagnosis of fetal growth restriction.

Such findings are supported by other studies looking at the factors associated with stillbirth in the general population. In a Swedish database of over 300,000 births, babies with a weight <10th customised percentile had a 6 fold increased risk of being stillborn [2].

The close link between fetal growth restriction and stillbirth places increased emphasis on improved antenatal surveillance. This can be achieved by longitudinal assessment of fundal height supported by ultrasound biometry and assessment by Doppler to determine which fetus is at risk and in need of delivery from an unfavourable intrauterine environment.

1. Classification of stillbirth by relevant condition at death (ReCoDe): population based cohort study. *Br Med J* 2005;331:1113-1117.

2. Perinatal outcome in SGA births defined by customised versus population based birthweight standards. *Br J Obstet Gynaecol* 2001;108:830-4.

Medical Conditions and the Risk of Stillbirth

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Approximately 10% of stillbirths are associated with maternal conditions. Late fetal deaths are associated with maternal medical conditions that are potentially preventable. Hypertensive disorders, diabetes, lupus, antiphospholipid syndrome, inherited thrombophilia, renal disease, thyroid disease, and obesity have all been associated with an increased risk of stillbirth. Through optimal management the rates of stillbirth have decreased significantly for some of these conditions. There is an increased risk of stillbirth associated with the development of intrauterine growth restriction (IUGR) in pregnancies complicated by hypertension, preeclampsia, antiphospholipid syndrome, and inherited thrombophilia. The patho-physiology of IUGR involves elevations of placental blood flow resistance, changes in regional blood flows, and alterations in fetal

cardiac functioning. Doppler studies correlate with the severity of IUGR. Identification and optimal management of fetal growth restriction via ultrasound, Doppler studies and antepartum fetal surveillance will be reviewed in this presentation. These clinical studies have reduced the risk of stillbirth in pregnancies complicated by IUGR.