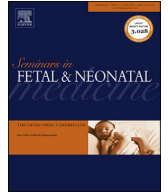




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Pregnancy subsequent to stillbirth: Medical and psychosocial aspects of care

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Pregnancy after stillbirth presents unique challenges for families and healthcare providers. Medical surveillance and interventions must be optimized to improve outcomes and provide individualized support for families. A key component of acceptable care is psychosocial support that is delivered in a timely and sensitive manner by care providers with knowledge about the pervasive impact of stillbirth. With the lack of existing evidence to guide care, there is an urgent need for global leadership and research to address knowledge gaps.

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1. Introduction

It is estimated that 2.6 million third-trimester stillbirths occurred worldwide in 2015, with most occurring in low- and middle-income countries [1]. Stillbirth has a pervasive impact on women, families, health systems, and communities. This impact continues into the subsequent pregnancies. After perinatal loss, the majority of women become pregnant again, with rates of pregnancy as high as 80% within the first 18 months [2,3]. It is important that healthcare providers understand the impact of stillbirth on subsequent pregnancies in order to promote the health and wellbeing of the fetus, neonate, woman, family, and community.

2. Pregnancy care systems

2.1. The good news: the value of specialized care

There is increasing evidence that informed, sensitive, and specialized care may have a powerful positive influence on women who are pregnant following stillbirth. Women report increased satisfaction when given the option of primary care or regular input from knowledgeable and specialized providers, including

obstetricians, nurses, and midwives [2,4–6]. In our Subsequent Pregnancy Program at Sunnybrook Health Sciences Centre in Toronto, Canada, we also find that families need individualized care plans and knowledgeable navigation throughout pregnancy and the postpartum period by a known interprofessional team.

2.2. The current system: a call for change

There is increasing evidence that women experiencing pregnancy after stillbirth have unique care needs. Existing obstetrical management practices do not sufficiently address these needs and families are not satisfied with traditional models of hospital antenatal care [3,5–8]. In a pregnancy after stillbirth, many women seek reassurance through interactions with providers, but report that interactions often fall short of their expectations [3,5,9]. Many parents encounter providers who are unaware of their history and the relevant impact of stillbirth, have dismissive attitudes to worries and concerns, and make insensitive and inappropriate comments [3].

Whereas some authors reported positive evaluations of specialist programs and support, including telephone contact, increased and flexible appointments, individualized preparation for birth, parent education, and postnatal support [3], others noted that specialized care is inconsistent [5,6,9]. Additionally, whereas targeted support appears to improve experiences for families, the contribution of different interventions to the overall success of programs is not clear [3].

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2.3. Moving forward: challenges for care providers

Counseling regarding management of a subsequent pregnancy is a great challenge, as little evidence is available to guide providers in this setting. Understanding and addressing the unique needs of families is important for care providers, but current guidance is lacking, as are evidence-based care pathways [2,3,5,10–12]. Guidelines that address individual risk factors, local conditions and resources, and the psychosocial needs of families are necessary [10,11,13].

3. Preconception counseling and the inter-pregnancy interval

There is no recommended regimen for the right inter-pregnancy interval after a stillbirth. Women should generally be encouraged to pursue pregnancy if and when they feel the time is appropriate [9,14].

Parent groups and practitioners have encouraged preconception counseling. At this time, a review of the index event can be conducted, a thorough history can be ascertained, and expectations in the subsequent pregnancy can be established. There is often a significant amount of anxiety that comes with attempts at conception following a stillbirth, and visits during the inter-pregnancy interval, reassurance of management plans, and surveillance are helpful for parents [15].

4. Risk of recurrent stillbirth

There is conflicting evidence regarding the risk of subsequent stillbirth. Whereas some authors have suggested that there is a low risk for recurrence when the index stillbirth is truly unexplained [16], others have shown increased risk of stillbirth in subsequent pregnancies, ranging from two-to ten-fold over the general population [17,18]. Much of this depends on the etiology of the index stillbirth, the degree of investigation of the index event, and level of intervention to correct medical disorders. Retrospective studies provide varying data on the risks of recurrent of stillbirth and are limited by inconsistency in defining the index stillbirth [19].

Increased recurrence risks have been shown in women with first trimester losses, early and late stillbirths, and intrapartum deaths. These risks remained significant among women perceived as otherwise low risk, indicating that unless there is an obvious, non-reproducible cause of the initial stillbirth, there is a baseline risk of recurrence that requires attention in the subsequent pregnancy [20]. Other studies showed these risks to be most pronounced among women for whom the index stillbirth was in the extreme preterm period or post term [21].

A recent meta-analysis [22] echoed the results of individual studies. Pooled data from cohort and case–control studies showed a five-fold increase in the odds of stillbirth in subsequent pregnancies. The higher risk of recurrence may be among those with placental or growth-related issues in the index pregnancy. Indeed, when looking at recurrence based on etiology, it has been shown that women who sustain a pregnancy loss due to placental factors or due to prematurity are at highest risk of recurrence [23]. We find that women who fall into these categories, especially when placentally mediated, are often categorized as having unexplained or unexplored stillbirths.

An increased rate of gestational diabetes in the subsequent pregnancy, reduced birth weight, earlier deliveries, increased risks of fetal distress, and increased rates of obstetric intervention were also all shown in subsequent pregnancies [16]. One challenge for providers when assessing recurrence risk is that the finding of low recurrence for unexplained stillbirths, as some authors have suggested, may not be applicable when the “unexplained stillbirth” is

actually one whose etiology has not been thoroughly explored. Furthermore, the increased risk of poor subsequent obstetric outcomes could be due to underlying medical issues or iatrogenic from increased interventions.

It is important to note that many families are not reassured when considering their recurrence risk [15] and that their appraisal of threat to the pregnancy is often not connected to a determined medical risk [4,24]. Management of the subsequent pregnancy requires a balance of evidence-based recurrence risk with the acknowledgement that certain interventions will be required due to case-specific issues as well as parental anxiety.

The risks of recurrent stillbirth are mitigated by the resolution of certain modifiable risk factors. In high-income countries, these are usually smoking and obesity, whereas in lower-income countries this includes the provision of adequate antenatal and intrapartum care [25,26]. Because of the inherent medical and psychosocial complications and considerations, these pregnancies should be treated as high risk and commensurate with the specific care needs of the families involved [3,20,27].

5. Screening in the subsequent pregnancy

When a woman is seen prior to, or during, a subsequent pregnancy, a thorough history and exploration of the events of the stillbirth is helpful in considering the etiology and the risk of recurrence. The most valuable information regarding the cause of stillbirth is collected at the time of the event. At this time, a genetic survey, autopsy, autoimmune, and diabetes screening should be performed, in the hopes of identifying a possible cause. Thorough investigation of a woman's health and obstetrical history allows providers to anticipate and provide necessary care, including targeted supports and referrals [2,11]. Placental pathology merits consideration in all cases.

Women with an unexplained pregnancy loss after 10 weeks of gestation may warrant testing for antiphospholipid antibody syndrome (APLS). The laboratory criteria include the presence of one of the antibodies (lupus anticoagulant, anticardiolipin antibody, or anti- β_2 glycoprotein) on two occasions at least 12 weeks apart [28]. APLS predisposes to vascular thrombosis and increases risk of fetal death and growth restriction. When present, obstetrical outcomes are improved through treatment with anticoagulation and low-dose aspirin [28].

Biochemical markers in the first trimester may play a role in predicting the risk of stillbirth. The FASTER trial [29] showed an increased rate of stillbirth [odds ratio (OR): 2.15; 95% confidence interval (CI): 1.11, 4.15] and spontaneous loss prior to 24 weeks (2.50; 1.76, 3.56) where the PAPP-A (pregnancy-associated plasma protein A) taken during first trimester screening was below the 5th percentile in pregnancies unaffected by chromosomal abnormalities. A prospective study looking at prediction of risk of stillbirth at greater than 24 weeks based on first-trimester testing showed lower PAPP-A levels in women who sustained stillbirth in general, especially when for presumed placental reasons [30].

Failure of normal invasion of spiral arteries and subsequent risk for placental dysfunction may be displayed by abnormal uterine artery Doppler studies. It is not yet certain at which gestation this should commence or at what frequency they should continue [18].

First-trimester uterine artery Doppler studies may help identify pregnancies at risk for poor perinatal outcomes. A recent prospective study [31] assessing risk of adverse outcomes, including stillbirth, with low PAPP-A and abnormal uterine artery Dopplers found an association with low sensitivity. In the second trimester, a recent randomized controlled trial showed an increased risk of stillbirth with elevated uterine artery Doppler resistance [32]. Similarly, a meta-analysis of studies looking at the prediction of

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