

Investigating stillbirths using a simplified obstetric events-based protocol

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ABSTRACT

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.

Keywords: autopsy, obstetric protocol, placental biopsy, stillbirth

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INTRODUCTION

An intrauterine death, often unexplained⁽¹⁾, is a distressing event for both parents and clinicians, particularly in this era of planned parenthood. While society displays an increased awareness of sudden infant death syndrome (SIDS), less attention has been focused on unexplained antenatal stillbirths that

represent the majority of perinatal deaths⁽²⁾. While arguments regarding the definition of stillbirths persist, there is even less consensus regarding the type of tests that are required in the work-up of a foetal death. Various papers have evaluated protocols for postmortem examination, but few reports describe a protocol for the investigation of stillbirths.

Our hospital devised a standard protocol for stillbirth investigations in 1999. Components of the protocol were selected with emphasis on the most common identifiable causes of stillbirth in our hospital^(3,4). The objective of this study was to evaluate this obstetric events-based stillbirth protocol in determining: (a) a cause for the stillbirths, (b) compliance of attending physicians, and (c) the usefulness of the various components of the protocol.

METHODS

A stillbirth was defined as the delivery of a foetus beyond 28 weeks gestation with no signs of life. Investigations were initiated upon diagnosis of the intra-uterine death. The protocol is outlined in Fig. 1. Parents were also counselled for a postmortem examination of the foetus. If consent for the postmortem was withheld, pathological examination of the placenta would be encouraged. There is no consensus regarding the ideal classification for stillbirths. Authors have used various classifications, such as the Extended Wigglesworth, Foetal/ Neonatal Factors, the Obstetric (Aberdeen) and the Obstetric (KKH Singapore) classifications. Each has its own merits⁽⁴⁾. The Obstetric (KKH Singapore) classification, which was more clinically oriented, formed the basis for the development of our protocol in this study (Table I).

All stillbirths managed in our hospital between 1 January 2000 and 31 December 2000 were analysed. These included unbooked cases (cases with no prior antenatal care) as well as in-utero cases that were diagnosed in other hospitals but transferred to our hospital for further management. Our stillbirth protocol was instituted upon diagnosis of the intra-uterine death as we anticipated a delay in the interval to delivery, particularly in cases of multiple pregnancies.

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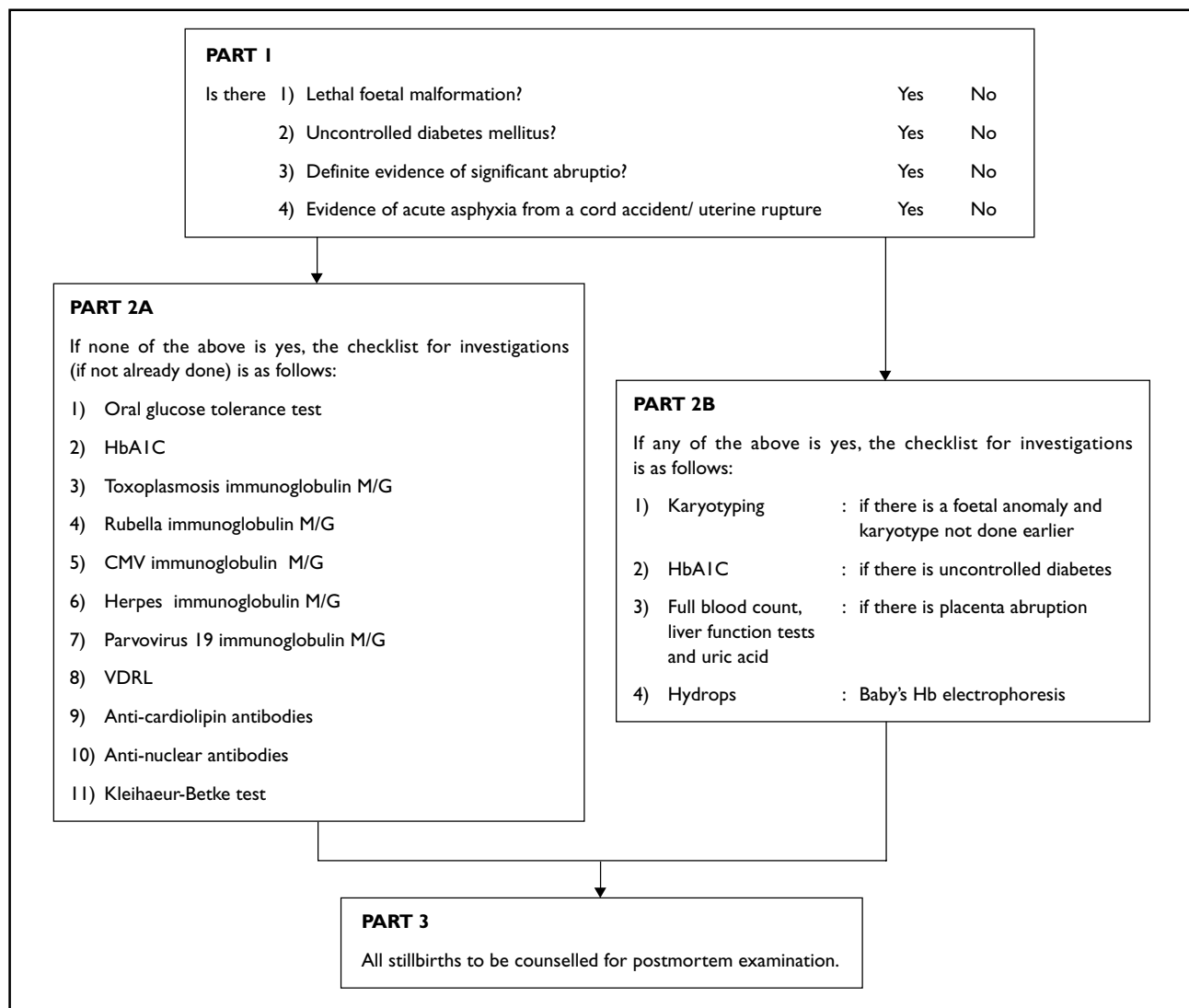
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Fig. I Flow chart shows KK Hospital's simplified obstetric events-based protocol for the investigation of stillbirths (non-corer's cases).**Table I. Causes of stillbirths (according to the Obstetric KKH Singapore classification).**

Causes	n=61	%
1 Unexplained	23	37.7%
2 Lethal malformations	10	16.4%
3 Uncontrolled diabetes mellitus	9	14.8%
4 Hypertensive disease resulting in abruption or IUGR or eclampsia	1	1.6%
5 Abruptio placentae- other than due to hypertensive disease	3	4.9%
6 IUGR- other than due to hypertensive disease	2	3.3%
7 Cord accident/ prolapse/ abnormality	8	13.1%
8 Infection/ chorioamnionitis	3	4.9%
9 Fresh stillbirth from acute asphyxia, ruptured uterus or trauma	0	0%
10 Foetal or maternal haemorrhage	0	0%
11 Twin-to-twin transfusion sequence	1	1.6%
12 Post-maturity	0	0%
13 Hydrops	0	0%
14 Others- antepartum asphyxia	1	1.6%

The protocol was introduced to all hospital staff in 1999 and was easily accessible in all antenatal, gynaecological and labour wards. Each stillbirth was discussed at our department's perinatal mortality meeting. Data pertaining to the patient's epidemiological characteristics, antenatal progress and stillbirth characteristics were summarised into a structured format and peer-reviewed by two consultant obstetricians.

Epidemiological characteristics included maternal age, race, gravidity, parity, and type of gestation. Stillbirth characteristics included gestational age, booking characteristics, birthweight, sex, type of stillbirth, mode of delivery, cause of the stillbirth, interval to delivery, and postmortem rates. At delivery, the presence of any dysmorphic features, placental weight and umbilical cord length were noted. Protocol compliance, reasons for any deviation and the usefulness of the various components of the protocol

Table II. Comparison of the stillbirth population with the KK hospital population.

Epidemiological characteristics		Hospital population n=16980		Stillbirth population n=61		Stillbirth rate (per 1000 total births)
			(%)		(%)	
Age: *(p<0.001)	>30 years	6647	39.1%	39	63.9%	2.2
	<30 years	10327	60.8%	22	36.1%	4.2
	unknown	6	0.1%	0	0	
Race: *(p=0.005)	Chinese	9469	55.7%	22	36.1%	2.3
	Malay	4789	27.9%	23	37.7%	4.8
	Others	2722	16.4%	16	26.2%	5.9
Parity: *(p=0.435)	Nulliparous	6952	40.9%	22	36.0%	3.2
	Multiparous	10028	59.1%	39	64.0%	3.9
Gestation *(p=0.014)	Singleton	16583	97.7%	56	91.8%	3.4
	Multiple	397	2.3%	5	8.2%	12.4
Gestation *(p<0.001)	>40 weeks	3724	21.9%	4	6.6%	1.1
	36-39 weeks	12238	72.0%	26	42.6%	2.1
	34-35 weeks	527	3.1%	7	11.5%	13.1
	26-33 weeks	418	3.0%	24	39.3%	54.3

* Fisher exact chi square test.

were analysed. Protocol compliance was defined, by the protocol, as the patient having had all the appropriate investigations up to the stage of counseling for postmortem examination.

The decision to undertake the postmortem was left to the parents' discretion and was not considered within the realm of compliance with the protocol. SPSS for Windows software version 11.0 (Chicago, IL, USA) was used for data analysis. Statistical analysis was done using the two-tailed Fisher exact test; $p < 0.05$ was considered to be significant.

RESULTS

There were 61 cases of stillbirths among 16980 births in the one-year study period (3.6 per 1000 births). The corrected stillbirth rate (>1000g) was 3.1 per 1000 births. The mean maternal age was 31.4 years. 63.9% of the stillbirths occurred in women 30 years and older (39 of 61 cases). The corrected stillbirth rate was 2.2/1000 total births in women less than 30 years of age and 4.2/1000 total births in those 30 years and older ($p < 0.05$). The stillbirth rate was 2.3/1000 births in the Chinese population, 4.8/1000 births in Malays, and 5.9/1000 births in the other races. The mean gravidity was 3.2 for Chinese, 4.9 for Malays, and 2.8 for the other races. There were four twin pregnancies and one triplet pregnancy (Table II).

42 women (68.9%) received antenatal care, of which 38 (62.3%) had antenatal care before 24 weeks. There were eight unbooked cases (13.1%) and four cases (6.6%) which were transferred in from private hospitals as intra-uterine deaths. Seven cases (11.5%)

defaulted their subsequent follow-up in the third trimester. The majority of stillbirths (52.5%) weighed more than 1999g, 34.4% were between 1000 to 1999g, and 13.1% were less than 1000g. There was no difference in the sex ratio of the stillbirths. 85.2% of the stillbirths were macerated and 77.0% were delivered vaginally.

The causes of the stillbirths are summarised in Table I. The interval from diagnosis of the intra-uterine death to time of delivery ranged from 0 to 33 days, with a mean of 2.2 days and a median of 1 day. The longest interval of 33 days occurred in a woman with the twin-to-twin transfusion syndrome (Table III). Investigations were initiated before the delivery of the stillbirth in seven out of eight cases of cord accidents that were compliant with the protocol. By our protocol, 33 of the 61 cases (54.1%) required the full panel of tests while 18 cases (29.5%) required selected investigations. These 51 cases were compliant with the protocol (83.6%) (95% CI 74.4%-92.8%). Protocol deviation occurred in the remaining 10 cases (16.4%) of which seven (11.5%) were over-investigated.

The seven over-investigated cases comprised two lethal malformations (Trisomy 18 and Ebstein's anomaly) that had declined pregnancy termination, one placental abruption and four women with gestational diabetes. Three of the diabetic patients were poorly compliant with their insulin and follow-up visits, while a fourth with impaired glucose tolerance defaulted follow-up in her third trimester – all of whom delivered macrosomic foetuses. Further investigations of the three under-

investigated cases were deemed unnecessary by their attending obstetricians.

The first case involved a dichorionic twin pregnancy with an intra-uterine death of one twin at 30 weeks gestation. An obvious cord accident of the first twin was noted at delivery of the second twin at 34 weeks. The second case involved a trichorionic triplet pregnancy conceived via in-vitro fertilisation (IVF) in which the remaining twins were delivered a week later, at 29 weeks, following abnormal Doppler ultrasonography results – no obvious cause of death was detected at delivery and only consent for placental examination was given. The third case involved a placental abruption but in the absence of raised blood pressure and albuminuria, biochemical evidence of pre-eclampsia was not obtained.

Selected investigations would have sufficed in all of the seven over-investigated cases and in the case of the placental abruption. An overall cost reduction in 26 cases (42.6%) could have been achieved if these eight cases had only selected investigations performed. Protocol deviation was appropriate in only three of the 10 cases – these three cases comprised the under-investigated group (30.0%).

The overall postmortem (PM) rate was 27.9%. Uptake for PM examination was dependent on parental consent: the majority of parents declined to have a PM (72.1%). Although the Malay population had a higher stillbirth rate (4.8/1000 total births) compared to the Chinese population (2.3/1000 total births), they had a much lower PM rate (5.9%) than the Chinese ($p=0.005$).

Of 45 patients who had the oral glucose tolerance test, five (11.1%) had abnormal results – of which three had impaired glucose tolerance and two were newly-diagnosed diabetics. This was based on the World Health Organisation (WHO) criteria, following a 75g glucose load of ≥ 11.1 mmol/L for a diagnosis of diabetes mellitus and ≥ 7.8 mmol/L for a diagnosis of impaired glucose tolerance⁽⁵⁾.

Antibody titre levels for congenital infections were positive in four of 41 cases (9.8%) but placental and PM findings were only able to support a diagnosis of congenital infection in one case (2.4%). The four cases were found to have positive serology for Parvovirus, *Herpes simplex* virus, Cytomegalovirus and Syphilis, respectively. Auto-antibodies were positive in two of 41 cases (4.9%). The Kleihauer-Betke test was negative in all 27 cases that were tested for foeto-maternal haemorrhage.

DISCUSSION

With the improvement in the standard of neonatal care in Singapore, there has been greater interest in

Table III. Interval from diagnosis to delivery.

Interval to delivery (days)	n=61	%
0	24	39.3
1	17	27.9
2	11	18.0
3	1	1.6
4	2	3.3
≥ 5	6	9.8

stillbirths and neonatal deaths. The investigation of stillbirths can highlight causes and suboptimal factors that may be present in patient management, provide possible answers to distressed parents and obstetricians alike and form the basis for better antenatal care in subsequent pregnancies⁽⁶⁾. Our protocol for the investigations of stillbirths was devised to assist in this aspect, and to standardise the type of investigations required to enable useful and cost-effective information to be obtained for both the patient and health-care system.

In our study, no identifiable cause could be detected in 22 cases (37.7%) of the stillbirths. This is comparable to other studies^(2,3,7-9). In their respective analysis of stillbirths, Morrison et al⁽⁷⁾ reported 19% of cases had unclassifiable stillbirths while Pitkin⁽⁸⁾ estimated that approximately 50% of foetal deaths beyond 20 weeks gestation were unexplained. Fretts et al⁽⁹⁾ reported more than 25% rate of unexplained stillbirths.

Compliance with the protocol occurred in 51 cases (83.6%) (95% CI 74.4% -92.8%), whereas deviation from the protocol occurred in 10 cases. Non-compliance with the protocol highlights the importance of frequent reinforcement and education of all staff and the role of individualisation of management. This is illustrated by the comprehensive panel of tests requested by some obstetricians and patients to help them cope with their subsequent grief and in cases of pregnancies conceived via assisted reproductive techniques, procedures known to be associated with substantial stress⁽¹⁰⁾ and increased perinatal mortality rates. In such cases, couples may understandably be against having further tests performed, although the implications of withholding tests should be highlighted as changes in mindset do occur at postnatal visits.

We found that the cost-effectiveness of this protocol could be influenced by factors such as familiarity with its components, the timing of the institution of the protocol, and the patients' religious sentiments. By instituting the protocol post-delivery, causes such as cord accidents (which comprised

13.1% of the causes of our stillbirths) would then become evident, thereby negating the need for further investigations. Our data also showed that the mean interval to delivery from the initial diagnosis was two days, with most deliveries occurring within the same day of diagnosis of the intrauterine death (Table III).

Delaying the institution of the protocol until the delivery of the stillbirth would therefore not be inappropriate. This, however, would be at the expense of emotional dissatisfaction of anxious parents who may want appropriate action to be expediently carried out to detect any abnormalities. A good stillbirth protocol not only helps in elucidating the cause of death but also aims to minimise unnecessary investigations, thus keeping healthcare costs to a minimum and ensuring optimal patient care. Although our protocol helped to minimise costs in 29.5% of cases, a further reduction to 42.6% could have been achieved with improved protocol compliance.

The importance of the postmortem in the evaluation of a foetal death has been emphasised in several studies⁽¹³⁻¹⁶⁾. Postmortems led to the clinical diagnosis being revised in 12% of otherwise apparently-unexplained stillbirths that weighted more than 1kg in the 1999 confidential inquiry into sudden deaths in infancy (CESDI report)⁽¹¹⁾. The American College of Obstetricians and Gynecologists states that "a carefully performed autopsy is the single most useful step in identifying the cause of fetal death" and includes foetal and placental examinations in its algorithm for foetal demise management⁽¹²⁾.

Our post-mortem rates were only 27.9%. Although the Malay population had a higher stillbirth rate compared to the Chinese, this group had the lowest post-mortem rates (5.9%). These uptake rates were expectedly divergent in view of the religious beliefs and cultural differences between the races. The usefulness of the post-mortem in our local population is limited, as the uptake rate has always been poor among certain groups of our population^(3,4,17). In spite of these rates, the value of the postmortem cannot be understated⁽¹⁴⁻¹⁶⁾.

Muller et al⁽¹³⁾ suggested that when resource are limited, gross postmortem examination, photography and radiography should be performed for all cases, with selective use of karyotyping and histopathology to minimise the use of expensive, low yield procedures. Furness et al⁽¹⁸⁾ used ultrasonography to visualise the foetal brain, heart, lung and kidneys in cases where postmortems were withheld. Recently, Alderliesten et al⁽¹⁹⁾ studied the value of magnetic resonance (MR) imaging as an alternative to postmortem examination and found that acceptance

rates for MR imaging only were better but that diagnostic accuracy was insufficient to recommend substitution of the full postmortem. To circumvent the low acceptance rates for the postmortem in our population, alternative options may lie with the use of photographs (which enable various views and close-ups of an abnormality to be taken), total body radiographs (particularly in cases of asymmetrical intra-uterine growth retardation or skeletal dysplasias), or ultrasonography.

The other components of our protocol included tests for congenital infections, autoimmune conditions and foeto-maternal haemorrhage. 9.8% had positive screens for congenital infections but placental and postmortem findings were only able to support the diagnosis in one case (2.4%). Evidence in the literature appears to support our findings. Benirschke et al⁽²⁰⁾ and Incerpi et al⁽²¹⁾ reported that congenital viral infections were uncommon causes of foetal death. Given this, Incerpi et al⁽²¹⁾ no longer recommended routine screening for congenital infections in their protocol. Nevertheless, we feel that a negative result is important as it can help to exclude congenital infections as the likely cause of the stillbirth and help allay parental anxiety. Our study also showed that two of 41 cases (4.9%) had autoimmune antibodies although in both cases, an autoimmune disorder was not implied as the cause of the stillbirths.

The evidence in the literature^(22,23) demonstrates a direct association of anti-phospholipid antibodies with foetal death. Laube and Schaubberger⁽²⁴⁾ reported that 13.8% of their cases resulted from foeto-maternal haemorrhage while Pitkin⁽⁸⁾ recommended a Kleihauer Betke test in all cases of unexplained stillbirths. We were not able to demonstrate similar results in our series. In our study, 11.1% had abnormal glucose tolerance test results and 14.8% of the causes of our stillbirths resulted from poorly-controlled blood sugar. As such, the glucose tolerance test remains an important part of the protocol⁽⁵⁾.

We feel that it is important for the investigation of stillbirths to be tailored according to significant preceding obstetric events. Our simple obstetric events-based protocol for investigations can be adapted for other hospitals from different countries or regions. Modifications are necessary in view of differences in causes of stillbirths, local population preferences and cultures, technology and financial resources. This study highlights that the cause of most stillbirths continues to be elusive. It demonstrates the importance of good protocol compliance and how the protocol can be improved by familiarity with the protocol and fine-tuning the initiation of investigations.

The usefulness of the postmortem is limited by our low uptake rates. Photography and radiography may be pertinent in our local population as valuable information can be obtained by these simple and non-invasive tests. Deviations from the protocol do occur and there may be a role for further individualization of tests. Screening for congenital infections and autoimmune diseases produced low positive yields, but still played a role in excluding possible reasons for the stillbirth. Hospitals in developing countries with limited resources may therefore limit or change some screening components for congenital infections and autoimmune diseases to ensure that the investigations are cost-effective and stay relevant to its population.

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