Factors influencing the availability of a local hospital guideline on maternal care and fetal post-mortem work-up after antepartum stillbirth – A national survey

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#### Abstract

Objective: To describe the use of local hospital guidelines on maternal care and fetal post-mortem work-up following intrauterine fetal death (IUFD) in Austria and to evaluate epidemiological factors influencing the availability of such in secondary and tertiary referral hospitals Design: Prospective national survey Setting: 75 secondary and tertiary referral hospitals providing obstetrical care in Austria Population: Obstetrical departments Methods: National survey with a paper-based questionnaire covering nine general questions regarding local hospital facilities and four comprehensive questions regarding medical approach following IUFD Main Outcome measures: Epidemiological data Results: 46 (61.3%) obstetrical departments [37 (80.4%) secondary; 9 (19.6%) tertiary referral hospitals] participated in this survey, of which 17 (37.0%) had local hospital guidelines on care after IUFD, whilst 29 (63.0%) denied. Availability of a local guideline was strongly correlated with the regular practice of post-mortem consultations (p=0.012). 16 (34.8%) hospitals replied to always schedule a follow-up consultation with affected parents, whilst 7 (15.2%) denied. In 8 (17.4%) hospitals post-mortem consultations would only be scheduled, if post-mortem examinations had been conducted. Neither type of institution (p=0.613), on-site pathology department (p=0.177), nor institutional annual live birth (p=0.291) and stillbirth rates (p=0.438) were found to influence the availability of local hospital guidelines. 26 (56.5%) participants considered a national guideline on IUFD necessary. Conclusion: Less than half of the surveyed institutions, regardless of annual live- or stillbirth rate and type of referral centre, have implemented a local guideline at their department. Availability of such may be influenced by regular conduction of post-mortem follow-up consultations.

# MANUSCRIPT

#### INTRODUCTION

Antepartum stillbirth or intrauterine fetal death (IUFD) is defined as the fetal death in utero from 20 gestational weeks onwards and affects approximately 1.3 million pregnancies worldwide and about 3 in 1000 live births in Central Europe. Stillbirth is a devastating event and may harbor risk factors with the potential to recur in future pregnancies. It is therefore warranted to elucidate the cause of fetal death in each case to prevent further harm. Professional guidelines for maternal care and fetal post-mortem work-up after IUFD are available from national societies such as the Royal College of Obstetricians and Gynaecologists (RCOG), the Perinatal Society of Australia and New Zealand (PSANZ)<sup>3, 4</sup> and the America College of Obstetrics and Gynaecology (ACOG). Common components in the post-mortem work-up are the investigation of the placenta, fetal autopsy and maternal examinations, such as the Kleihauer-Betke test, glucose tolerance test, thyroid function tests, screening for infections and thrombophilia, as they have shown to reveal the cause of fetal death in up to 90%.

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To date, none of the German speaking European countries (Austria, Germany and Switzerland) have introduced a national stillbirth care bundle, yet there may be local guidelines in individual institutions. By this study we aimed to determine how many secondary and tertiary referral hospitals with obstetrical facilities have implemented a local guideline on maternal care and fetal post-mortem work-up after antepartum still-birth at their institution in Austria. We furthermore sought to identify epidemiological factors supporting the availability of such across the country. Our hypothesis was that hospitals with higher annual numbers of live and stillbirths, respectively, were more likely to have established a local standardized pathway for better maternal care.

## MATERIAL AND METHODS

#### Data collection

We created a 12-item questionnaire covering demographic variables (3 items), local facilities and practice following IUFD (5 items), routine post-mortem work-up (1 item) and obstetrical care after IUFD (3 items; **Appendix S1**). The questionnaire was sent out to all Austrian secondary and tertiary referral hospitals with maternity units (n=75) along with an invitation letter addressed to the departmental director and a franked response envelope. Survey time was between January and July 2019 and deadline was set after 2 months of receipt. Returned questionnaires were extracted for all variables and answers were transferred into an excel file sheet. Institutional epidemiological data were retrieved from the Department of Clinical Epidemiology Tirol Kliniken, Austria, and combined with our dataset. After data check for integrity and consistency, the database was frozen and made anonymous prior to final analysis.

#### Statistical analysis

Distribution of data was analyzed using the Kolmogorov-Smirnov test. Categorical data are given as counts (n) and percentages (%). Continuous data were compared with unpaired t-test and Mann-Whitney U-test, respectively. Categorical data were compared with  $\mathrm{Chi}^2$  and Fisher's Exact test, respectively. Relationships between continuous variables were assessed by Spearman's rank correlation tests. All reported p-values are two-sided, and a Greenhouse-Geisser corrected p-value was considered as level of significance (p <0.05) with a 95% confidence interval (CI). Statistical tests were performed with SPSS® Statistics Version 26.0.0.0 (IBM Corporation ©, Armonk, NY, USA) and figures designed by GraphPad Prism 8 for macOS Version 8.4.2 (GraphPad Software, LLC).

The study was approved by the Ethics Committee of the Medical University of Vienna (3<sup>rd</sup> August 2018) and complied with the principles as outlined in the declaration of Helsinki. Participants' written consent was not required per Austrian Federal Act concerning Protection of Personal Data (DSG 2000).

## RESULTS

## Baseline demographic characteristics

In total, 46 (61.3%) obstetrical departments from 37 (80.4%) secondary and 9 (19.6%) tertiary referral hospitals, respectively, participated in this survey. The survey covered eight from nine Austrian federal states [5 (10.9%) hospitals from the capital Vienna; 16 (34.8%) from Lower Austria; 8 (17.4%) from Upper Austria; 6 (13.0%) from Tyrol; 4 (8.7%) from Styria; 3 (6.5%) from Vorarlberg; 2 (4.3%) from Salzburg and 2 (4.3%) from Carinthia]. Annual live birth rate was [?] 500 in 5 (10.9%) participating hospitals, 501-1000 in 18 (39.1%) hospitals, 1001-2000 in 14 (30.4%) hospitals and [?] 2001 in 9 (19.6%) hospitals. Type of hospital (secondary versus tertiary referral hospital) significantly correlated with the presence of a local pathology department on site (p = 0.003) and the conduction of a post-mortem fetal magnetic resonance imaging (MRI; p = 0.016) in the participating units.

#### Availability of hospital guidelines

17 (37.0%) enrolled hospitals had local hospital guidelines on maternal care and fetal post-mortem work-up at their institution, whilst the majority of participants (n=29; 63.0%) denied. All participants (n=46; 100%), however, would deliver a woman after confirmed diagnosis of fetal death at their institution. 26 (56.5%)

participants consider that a national guideline on maternal care and fetal post-mortem work-up is required, whilst 13 (28.3%) denied and 7 (15.2%) did not disclose their interests.

#### Routine post-mortem consultations

16 (34.8%) hospitals replied to always schedule a routine post-mortem follow-up consultation with the parents, whilst 7 (15.2%) departments would never arrange a follow-up after the event of IUFD. In 8 (17.4%) hospitals post-mortem consultations would only be scheduled, if post-mortem examinations had been conducted. In 7 (15.2%) hospitals post-mortem consultations would only be arranged in case of suspicious or abnormal results and in 2 (4.3%) institutions, only if requested by the parents. 6 (13.0%) did not disclose their routine follow-up management after fetal death.

## Local facilities

Following diagnosis of IUFD, 8 (17.4%) institutions usually admit the woman to hospital for induction of labour (IOL) straight after diagnosis. 12 (26.1%) departments usually admit the woman on the following day, 3 (6.5%) on the following day or the day after and 4 (8.7%) departments would admit the woman after two days, as long as the woman is clinically stable. 19 (41.3%) institutions would place the decision regarding time of admission upon the woman's preferences. Interestingly, those institutions who kept the woman hospitalised straight after diagnosis of fetal death were more likely to perform maternal tests to rule out bleeding disorders, such as thrombophilia (p = 0.03) and a Kleihauer test (p = 0.049), yet also replied they considered a lack of a national guideline regarding post-mortem work-up after IUFD in Austria (p = 0.026).

All but one institution offer professional psychological support to affected parents whilst hospitalised and 9 (19.6%) departments also arrange psychological follow-up consultations as an out-patient.

In 21 (45.7%) participating institutions, a local pathology department is on site, whilst the majority of participating hospitals (n=25; 54.3%) have none. Presence of a local pathology was found to be strongly correlated with the type of the institution (p = 0.003) and therefore also annual live birth rates (p = 0.039). Furthermore institutions with an integrated department of pathology would perform more often fetal genetic tests after IUFD (p = 0.017).

#### Post-mortem examinations

Table 1 summarizes all types of requested maternal, placental and fetal post-mortem examinations following IUFD, independent of availability of a local hospital guideline, and compares their frequency between secondary and tertiary care hospitals. Whilst 44.4% of tertiary care hospitals would consider conducting a fetal MRI after fetal death, 89.2% of secondary care hospitals would never perform such (p=0.036). Likewise, significantly more tertiary referral hospitals would request chromosomal and microarray analysis following IUFD (44.4%) compared to secondary referral hospitals (19.4%;p=0.016). No other significant differences in routine post-mortem examinations were observed between secondary and tertiary referral hospitals. In summary, the three most common post-mortem examinations always conducted in Austrian maternity units following IUFD are placental histology (20.9%), fetal autopsy (13.1%) and maternal antibody screen (11.5%; Figure 1). Performance of fetal autopsy strongly correlated with the concomitant conduction of a fetal genetic test (p=0.015) and placental histology (p=0.031), yet was independent of the local facility of a department of pathology (p=0.341) and type of referral hospital (p=0.451).

## Induction of labour

In Austria, most common regime for IOL between  $24^{+0}$  and  $27^{+6}$  gestational weeks, yet also above  $28^{+0}$  gestational weeks is mifepristone on admission day (Day 1), followed by misoprostol on two subsequent days (73.9% and 23.9%, respectively; Figures 2 and 3).

Factors influencing availability of local hospital guideline on maternal care and fetal post-mortem work-up Availability of local hospital guideline on maternal care and fetal post-mortem work-up was found to be strongly correlated to regular conduction of post-mortem consultations (p = 0.012). However, neither type of institution (p = 0.613), on-site pathology department (p = 0.177), nor institutional annual live birth (p = 0.291) and stillbirth rates (p = 0.438), respectively, were found to influence the availability of local hospital guidelines.

## **DISCUSSION**

#### Main findings

In the absence of national guidelines on maternal care and post-mortem examinations following stillbirth in Central Europe, this is the first survey to investigate availability of local hospital guidelines in maternity units in Austria and to evaluate their practice in maternal care ranging from admission, psychological support and medication regime for induction of labour to post-mortem investigations and follow-up consultations. With an institutional response rate of 61 percent covering for 73% of all registered stillbirths and 64% of all registered live births in Austria, this survey provides a representative overview on practice and position.

Whilst we found that only a small proportion of hospitals have implemented clinical practice guidelines on stillbirth, we identified the routine practice of post-mortem consultations with the bereaved parents to be an influential factor for the availability of an IUFD care bundle. Whether this is the consequence of the guideline or whether patient-centred communication and care had subsequently supported formal establishment of a local guideline, remains open in this survey. After all, we dismissed our hypothesis, that annual stillbirth rates would be the strongest facilitator for implementation of an institutional guideline.

Interestingly, independent of the availability of a hospital guideline, we found that placental histology, fetal autopsy and maternal antibody screening were the three most common examinations conducted in all IUFD cases in maternity units. This supports previous reported uptake rates. In the United Kingdom (UK), fetal post-mortem examinations are carried out in about 44% of stillbirths<sup>6</sup> and in the United States, the uptake of autopsy has been reported as low as 35% in tertiary care centres and 13% in community hospitals.<sup>7</sup> After all, post-mortem examinations are the single most useful investigation after fetal loss, as they provide insight into the aetiology of fetal death in 22-76% of the cases.<sup>8</sup>, <sup>9</sup>

# Strengths and limitations

The high acceptance rate for participation in this survey provides a representative overview on obstetrical practice in Austria. Of note, we received a response of all university departments, representing the major delivery units for stillborn babies in Austria. Furthermore, the majority of returned questionnaires were fully completed, thus limiting the number of missing data. The absence of a formal local guideline does not rule out any other form of routine practice performed after IUFD at an institution, which is intrinsically shared by team members and verbally established. The strength of the questionnaire was to capture these practices and provide an overview on clinical care. The combination of institutional data from questionnaires with epidemiological data from the Austrian Birth Registry allowed us to interpret the results with greater detail by adjusting for the numbers of live and stillbirths per institution.

Our study is not devoid of limitations inherent to the failure to control for recall bias of responders and thus data accuracy from returned questionnaires. As over half of the responding institutions showed both a lack of a local guideline and their support for implementation of a national stillbirth care bundle, at the same time, we cannot rule out a certain degree of selection bias. Also, small hospitals with low numbers of stillbirths might not have participated in this survey for the shortage of valid data they might have considered for this analysis. Finally, our survey covered secondary and tertiary degree hospitals in Austria only, and the collected data might not be fully translatable into other countries due to different local facilities and medico-legal practice after perinatal death. These limitations clearly indicate that our findings need to be confirmed by a larger European study to enhance the robustness of these questionnaire results.

## Interpretation

Defining the cause of death helps bereaved parents in their grieving process, 10, 11 estimated the recurrence

risk in future pregnancies, serves mortality statistics and future public health interventions to reduce the number of perinatal loss.<sup>12</sup> Elucidating the cause and underlying risk factors through thorough and concise post-mortem investigations may therefore prevent future stillbirths.

Clinical Practice Guidelines are "statements that include recommendations intended to optimize patient care". 13 Whilst their aim is to enhance the medical practice of doctors and guide them along with evidencebased knowledge towards better patients' care, 14 studies have likewise revealed poor adherence in cases where guidelines are not based upon good evidence, <sup>15</sup>lead to over-treatment rather than "effective" treatment of a patient, <sup>16</sup> or when conflicts of interests of authors create a bias in clinical recommendations. <sup>17, 18</sup> Evidencebased clinical practice guidelines on maternal and fetal post-mortem examinations therefore ought to be implemented in every hospital in order to optimize, standardize and harmonize their practice according to national guidelines such a supported by the RCOG, PSANZ or ACOG with the aim of finding the cause of fetal death and improve maternal care in subsequent pregnancies. Ideally, sensitivity of postmortem examinations should be high with a low inter-rater variability in result interpretation in order to determine the underlying aetiology with high accuracy.<sup>2, 19</sup> Placental histopathology fetal autopsy and fetal genetic testing are considered the gold standards following stillbirth.<sup>20</sup>Known barriers to post-mortem examinations, however, are considered the parents' dislike of invasiveness, inefficient communication and lack of understanding of the purpose. 21 Contrarily, parents' desire for more information acts as a facilitator and it therefore lies within the responsibility of the caring obstetrician to propose the optimal post-mortem workup after stillbirth in a respectful way to be eaved parents. Obstetricians most commonly consent bereaved parents for perinatal autopsy, yet about 12.4% claim to lack training in counselling, after all.<sup>22</sup>

Although the annual stillbirth rate in Austria has held stable at around 3.1 stillbirths per 1000 live births beyond 24 gestational weeks for the last 12 years, <sup>23</sup> a reduction of 10-15% by 2025 is desirable. In the UK, the annual stillbirth rate of 4.7 per 1000 live births ranks among the highest in Europe, which led the UK Department of Health and Social Care support the National Health Service to reduce the stillbirth rates by 50% by 2025. In 2015, the national prevention programme "Saving Babies' Lives Care Bundle" has been introduced, comprising four measures: (a) reduction of smoking in pregnancy, (b) assessment of risk and surveillance in growth restricted fetuses, (c) raising awareness of reduced fetal movements and (d) effective monitoring during labour.<sup>24</sup> Subsequently, UK hospitals had to implement local maternity guidelines in order to follow these steps towards better maternal and fetal care and prevention of stillbirth. A recent study evaluated the local practice guidelines from 75 participating UK hospitals and found that whilst only the minority of 5.6% of evaluated guidelines were recommended for clinical use and 75% needed some modifications, 16.7% were not recommended at all. 25 Assessment of staff opinions on the use of their clinical guidelines revealed that over half considered the guidelines to offer higher quality care to women, yet 30% of staff claimed not to be able to follow their guidelines due to time issues, while 24% were not able to implement their recommendations at all. These limitations clearly indicate that the quality, content and perceived utility of guidelines need to be addressed internationally.

## **CONCLUSION**

In this national survey, less than half of the participating obstetrical institutions have implemented a local standardized care bundle after stillbirth, regardless of annual live or stillbirth rate and type of referral centre. Availability of a local guideline seems to be accompanied by the conduction of routine post-mortem follow-up consultations.

Further studies are needed to validate our results.

## Disclosure of interest

None declared. Completed disclosure of interests form available to view online as supporting information.

#### Contribution to authorship

All authors contributed to the conception, planning and carrying out of the research. DAM conceived and designed the study and wrote the first draft of this paper. SN, HL and VR helped with acquisition of data.

DAM, SN and HL conducted statistical analyses. SL, PH, HK and PK helped with design and conception. All authors contributed to critically revising the paper for important intellectual content and approved the final version to be published. All authors accept responsibility for the article as published.

## Details of ethical approval

The study was approved by the Ethics Committee of the Medical University of Vienna (3<sup>rd</sup> August 2018) and complied with the principles as outlined in the declaration of Helsinki. Participants' written consent was not required per Austrian Federal Act concerning Protection of Personal Data (DSG 2000).

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## SUPPORTING INFORMATION

**Appendix S1.** 12-item questionnaire sent out to 75 maternity units in Austria between January and July 2019 (*Translated from German into English*)

#### TABLES AND FIGURES

- Table 1. Summary on spectrum and frequency of performed fetal, placental and maternal post-mortem examinations following intrauterine fetal death in secondary and tertiary care hospitals (n=46) across Austria (frequency n; percentage %) and comparison of frequency between types of hospital (two-sided Fisher's Exact test; level of significance p< 0.05)
- Figure 1. Overview on post-mortem examinations always performed after intrauterine fetal death in maternity units, which took part in this survey
- Figure 2. Frequency of medications administered for induction of labour following intrauterine fetal death between  $24^{+0}$  and  $27^{+6}$  gestational weeks in Austria
- Figure 3. Frequency of medications administered for induction of labour following intrauterine fetal death above  $28^{+0}$  gestational weeks in Austria

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Table 1 Summary on spectrum and frequency of maternal, placental and fetal post-mortem examinations following intrauterine fetal death in secondary and tertiary care hospitals (n=46) across Austria (frequency n; percentage %) and comparison in frequency between type of hospital (two-sided Fisher's Exact test; level of significance p < 0.05).

POST-MORTEM EXAMINATION	POST-MORTEM EXAMINATION	POST-MORTEM EXAMINAT
FETAL	Fetal autopsy	Always
	. v	Under certain circumstances
		Never
	Fetal MRI	Always
		Never
		$Under\ certain\ circumstances$
	Fetal genetics	Always
		Under certain circumstances
		Never
	Genetic test	Chromosomal examination
		Chromosomes + Microarray
		Microarray examination
DICAENTA	TT:-4-1	Not disclosed
PLCAENTA  MATERNAL	Histology	Always
		Under certain circumstances
	Kloihauer testing	Never
	Kleihauer testing	Always Under certain circumstances
		Never
	Antibody screening	Never $Always$
	minory screening	Under certain circumstances
		Never
	Blood cultures for infections	Always
		Under certain circumstances
		Never
	Virology screen	Always
		$Under\ certain\ circumstances$
		Never
	Urine culture	Always
		$Under\ certain\ circumstances$
		Never
	Vaginal swabs	Always
		Under certain circumstances
	TT1 A 4	Never
	HbA1c	Always
		Under certain circumstances
	CTT	Never
	oGTT	Always
		Under certain circumstances
	Thymoid forestion tool	Never
	Thyroid function test	Always
		Under certain circumstances
	Thrombanhilia	Never
	Thrombophilia screening	Always

# POST-MORTEM EXAMINATION POST-MORTEM EXAMINATION POST-MORTEM EXAMINATION

 $Under\ certain\ circumstances$  Never





