PERINATAL ASPHYXIA AND ITS ASSOCIATED FACTORS AMONG PERINATAL MORTALITY IN KELANTAN FROM 2020 – 2022.

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by

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LIST OF SYMBOLS

%	Percent
n	Sample size
p	Probability value
<	Less than
>	More than
≤	Less than or equal to
≥	More than or equal to
±	Plus or minus
=	Equal to
-	Hyphen or range
α	Alpha (significant level)

LIST OF ABBREVIATIONS

AGA	Appropriate for gestational age
aOR	Adjusted Odd Ratio
AUC	Area under the curve
CI	Confidence Interval
HCW	Healthcare Worker
IQR	Interquartile Range
JEPeM	Jawatankuasa Etika Penyelidikan Manusia
LMIC	Low- and middle-income countries
MCH	Maternal and Child Health
MOH	Ministry of Health
MREC	Medical Research and Ethics Committee
MS	Microsoft
O&G	Obstetrics and Gynecology
OR	Odd Ratio
ROC	Receiver operation characteristic
SD	Standard Deviation
SDG	Susceptible Development Goals
SGA	Small for gestational age
SPSS	Statistical Packages for the Social Sciences
SU5MR	Stillbirth and Under-five Mortality
UNICEF	United Nations International Children's Emergency Fund
USB	Universal Serial Bus
USM	Universiti Sains Malaysia
WHO	World Health Organization

ABSTRAK

ASFIKSIA PERINATAL DAN FAKTOR-FAKTOR YANG BERKAITAN DENGAN KEMATIAN PERINATAL DI KELANTAN 2020-2022.

Latar Belakang Kajian: Kematian perinatal adalah salah satu isu utama kesihatan awam di peringkat global, dengan kematian neonatal menyumbang hampir separuh daripada kematian kanak-kanak di bawah umur lima tahun. Asfiksia perinatal merupakan penyumbang utama kepada kematian perinatal, terutama di negara-negara berpendapatan rendah dan sederhana. Asfiksia perinatal dilaporkan sebagai punca kedua terbesar kematian perinatal yang boleh dicegah di Malaysia. Walau bagaimanapun, beban khusus dan faktor-faktor yang berkaitan kematian asfiksia perinatal ini masih belum jelas di Malaysia umumnya dan di Kelantan khususnya.

Objektif: Kajian ini bertujuan untuk menentukan kadar asfiksia perinatal dan faktor-faktor yang berkaitan dengannya dalam kalangan kes kematian perinatal di Kelantan, Malaysia, dari tahun 2020 hingga 2022.

Metodologi: Ini adalah kajian keratan rentas yang telah dijalankan antara Disember 2023 hingga Jun 2024 berdasarkan kajian semula data kematian perinatal yang dilaporkan kepada Jabatan Kesihatan Negeri Kelantan dari tahun 2020 hingga tahun 2022. Data sekunder bagi kajian ini telah diperoleh dari Sistem Pemberitahuan Lahirmati dan Kematian Kanak-kanak di bawah Lima Tahun dan Borang Siasatan Lahirmati dan Kematian Kanak-kanak di bawah Lima Tahun. Sebanyak 397 kes kematian telah dipilih dengan menggunakan kaedah persampelan rawak mudah dengan menggunakan *Microsoft Excel.* Faktor-faktor sosiodemografi, obstetrik, dan intrapartum telah diambil daripada rekod dan dianalisis menggunakan analisa

deskriptif, regresi logistik mudah dan regresi logistik berganda untuk mengenal pasti faktor-faktor yang berkaitan dengan asfiksia perinatal.

Keputusan: Daripada 397 kes kematian perinatal yang dikaji, kadar asfiksia perinatal adalah 25.9%. Analisis multivariat menunjukkan bahawa ibu bukan Melayu (aOR=2.70, 95% CI : 1.18-6.22, *p*=0.019), ibu yang menghadiri temujanji susulan antenatal yang tidak mencukupi atau ibu yang tidak berdaftar (aOR=2.95, 95% CI : 1.66-5.22, *p*<0.001), kelahiran pramatang lewat (aOR=2.49, 95% CI : 1.20-5.18, *p*=0.014), dan kelahiran pembedahan *Caesarean* (aOR=2.52, 95% CI : 1.51-4.21, p<0.001) berkait secara signifikan dengan asfiksia perinatal.

Kesimpulan: Asfiksia perinatal menyumbang sebahagian besar daripada kematian perinatal di Kelantan, Malaysia. Faktor-faktor ibu, seperti ibu bukan Melayu, ibu yang menghadiri temujanji susulan antenatal yang tidak mencukupi atau ibu yang tidak berdaftar, kelahiran pramatang lewat dan kelahiran pembedahan *Caesarean* adalah signifikan dikaitkan dengan kematian perinatal yang disebabkan oleh asfiksia perinatal. Pengenalpastian faktor-faktor yang berkaitan ini boleh membantu penambahbaikan strategi dan intervensi masa hadapan seperti meningkatkan penjagaan antenatal, meningkatkan pengurusan intrapartum, dan memperkukuhkan keupayaan penyediaan penjagaan kesihatan. Ini dapat memperbaiki mutu perkhidmatan dan dapat membantu mengurangkan kematian yang berkaitan dengan asfiksia perinatal di negeri ini. Kajian lanjut diperlukan untuk meneroka penyebab yang mendasari dan membangunkan strategi khusus konteks untuk menangani beban kematian perinatal yang tinggi di Kelantan.

Kata kunci: Kematian perinatal, asfiksia perinatal, faktor risiko, Kelantan, Malaysia

ABSTRACT

PERINATAL ASPHYXIA AND ITS ASSOCIATED FACTORS AMONG PERINATAL MORTALITY IN KELANTAN FROM 2020 – 2022.

Background of the study: Perinatal mortality remains a significant public health concern globally, with neonatal deaths accounting for nearly half of all under-five deaths. Perinatal asphyxia is a major contributor to perinatal mortality, especially in low- and middle-income countries. Perinatal asphyxia is the second largest preventable cause of perinatal death in Malaysia. However, the specific burden and factors associated with this perinatal asphyxiation death are still unclear in Malaysia in general and in Kelantan in particular.

Objective: This study aimed to determine the proportion of perinatal asphyxia and its associated factors among perinatal mortality cases in Kelantan, Malaysia, from 2020 to 2022.

Methodology: This cross-sectional study was conducted between December 2023 and June 2024 based on a retrospective review of perinatal mortality data by the Kelantan State Health Department from 2020 to 2022. Secondary data for this study were obtained from the Stillbirth and Under-five Mortality Notification System and Stillbirth and Under-five Mortality Investigation Form. A total of 397 deaths were selected using a simple random sampling method using Microsoft Excel. Sociodemographic, obstetric, and intrapartum factors have been taken from records and analysed using descriptive analysis, simple logistical regression and multiple logistic regression to identify factors associated with perinatal asphyxia.

Results: Out of 397 perinatal mortality cases reviewed, the proportion of perinatal asphyxia was 25.9%. The multivariate analysis showed that non-Malay mothers

(aOR=2.70, 95% CI : 1.18-6.22, p=0.019), inadequate antenatal follow up or unbooked mothers (aOR=2.95, 95% CI : 1.66-5.22, p<0.001), late preterm birth (aOR=2.49, 95% CI : 1.20-5.18, p=0.014), and caesarean section deliveries (aOR=2.52, 95% CI : 1.51-4.21, p<0.001) were significantly associated with perinatal asphyxia.

Conclusion: Perinatal asphyxia accounts for a substantial proportion of perinatal mortality in Kelantan, Malaysia. Maternal factors, such as non-Malay mothers, mothers attending inadequate antenatal follow-up or unbooked mothers; late premature births and caesarean births are significantly associated with perinatal mortality caused by perinatal asphyxia. Identifying these related factors can help improve future strategies and interventions such as improving antenatal care, improving intrapartum management, and strengthening the ability to provide health care. It can also help to improve service quality and reduce the number of deaths caused by perinatal asphyxia across the country. Further research is needed to explore the underlying causes and develop context-specific strategies to address the high burden of perinatal mortality in Kelantan.

Keywords: Perinatal mortality, perinatal asphyxia, risk factors, Kelantan, Malaysia

CHAPTER 1

INTRODUCTION

1.1 Study background and significance

1.1.1 Perinatal mortality

Despite significant global progress in reducing childhood mortality since 1990, the rate of decline in neonatal mortality has been slower than the reduction in post-neonatal mortality among children under five. Tragically, approximately 6,400 infants still die every day, accounting for nearly 50% of all under-five deaths worldwide. Looking ahead, it is projected that around 26 million newborns will perish between 2019 and 2030, and the majority of these devastating losses could have been prevented (UNICEF, 2020). Infectious diseases, complications of prematurity, birth asphyxia, and congenital anomalies remain the leading causes of mortality in this vulnerable age group globally (WHO, 2023b).

Perinatal mortality is an important public health concern on a global scale. This indicator encompasses all fatalities, including stillbirths and early neonatal deaths occurring within the critical first week of life (McMicking *et al.*, 2020; Khobragade *et al.*, 2021b). Perinatal mortality is a crucial measure for evaluating the well-being of expectant mothers, new mothers, and newborns. It can also serve as an important indicator of the standard of care provided to women throughout pregnancy, delivery, and the postpartum period, as well as to newborns during their first seven days of life (Malaysian Healthcare Performance Unit, 2020).

1.1.2 Perinatal asphyxia

Perinatal asphyxia is a medical condition that disrupts the exchange of gases in the blood, resulting in hypoxemia and hypercapnia. This can lead to metabolic acidosis, which is a significant cause of morbidity and mortality in neonates and children. Perinatal asphyxia is closely related to hypoxic-ischemic encephalopathy, a serious condition that can result in adverse outcomes such as neonatal death, cerebral palsy, and cognitive and behavioural issues (Crovetto *et al.*, 2018).

Globally, perinatal asphyxia accounts for 11% of under-five child mortality worldwide, ranking as the third leading cause of death after preterm birth (17%) and pneumonia (15%) (WHO, 2015). It is also one of the three leading preventable and treatable conditions responsible for 80% of all newborn deaths (UNICEF, 2020). In Ethiopia, perinatal asphyxia was the second leading cause of perinatal mortality, contributing to 31.2% of deaths (Ethiopian Public Health Institute, 2014). The high burden of perinatal mortality, especially due to perinatal asphyxia, is a significant concern in many low- and middle-income countries (LMICs). Across sub-Saharan Africa and South Asia, an estimated one million babies die each year from intrapartum-related complications, including perinatal asphyxia and it is estimated to be responsible for up to 23% of neonatal deaths worldwide (Lee *et al.*, 2013),

Similarly in Malaysia, it is reported that perinatal asphyxia was the second leading cause of preventable perinatal mortality, accounting for 28.8% of cases (Family Health Development Division, 2022). According to a study conducted at a university hospital in Kuala Lumpur, Malaysia, the proportion of perinatal asphyxia over seven years from 2004 to 2010 was found to be 22.3% at their centre (Hassan *et al.*, 2013). The state of Kelantan, Malaysia, has shown consistently high perinatal

mortality rates in recent years, though the specific proportion of perinatal asphyxia-related deaths remains unclear (Family Health Development Division, 2023).

1.2 Problem Statement and Study Rationale

Malaysia has made substantial progress in improving maternal and child health outcomes, with a reduction in the under-five mortality rate from 16.9 per 1,000 live births in 1990 to 7.8 per 1,000 live births in 2022 (Bank, 2024a). However, disparities in perinatal mortality rates persist across different states, with Kelantan showing consistently higher rates compared to the national average of 6.5 per 1000 live births for perinatal deaths, despite concerted efforts (Family Health Development Division, 2023). Furthermore, Malaysia as a whole has not attained the Sustainable Development Goal (SDG) target indicator 3.2, which aims to eliminate preventable deaths among newborns and children under five years of age (WHO, 2023b).

Perinatal asphyxia is a leading cause of death worldwide, and many of these deaths are preventable. However, research into perinatal asphyxia and its causes in Malaysia, particularly Kelantan, is limited. Existing research has primarily focused on live births, leaving a significant gap in understanding the specific risk factors that contribute to perinatal asphyxia-related deaths. Identifying these risk factors is crucial. It can provide valuable information for developing targeted interventions at the district and state levels. This knowledge can guide appropriate actions to address the underlying causes of perinatal asphyxia deaths. Addressing this research gap has the potential to improve the effectiveness of prevention and intervention programmes by identifying the specific factors that make high-risk groups in Kelantan more vulnerable to perinatal asphyxia.

Furthermore, the study's findings can be used to develop customised strategies that address the needs of the local population. Understanding the causes of perinatal asphyxia deaths in Kelantan will provide the evidence required to design and implement tailored interventions. These interventions may include improving antenatal and delivery care services, identifying risk factors early, and training healthcare providers to better recognise and manage perinatal asphyxia.

1.3 Research Questions

1. What is the proportion of perinatal asphyxia among perinatal mortality in Kelantan?
2. What are the factors associated with perinatal asphyxia among perinatal mortality in Kelantan?

1.4 Research Hypothesis

Null Hypothesis (Ho) = There is no significant association between maternal factors and intrapartum factors with perinatal asphyxia among perinatal mortality in Kelantan.

Alternate Hypothesis (Ha) = There are significant association between maternal factors and intrapartum factors with perinatal asphyxia among perinatal mortality in Kelantan.

1.5 Research Objective

1.5.1 General Objective

To determine the proportion of perinatal asphyxia and its association factors among perinatal mortality in Kelantan for 2020 to 2022.

1.5.2 Specific Objectives

1. To determine the proportion of perinatal asphyxia among perinatal mortality in Kelantan for 2020 to 2022.
2. To determine the factors associated with perinatal asphyxia among perinatal mortality in Kelantan for 2020 to 2022.

CHAPTER 2

LITERATURE REVIEW

2.1 Perinatal mortality

Kelantan's perinatal mortality rate has been fluctuating over the past decade, but has shown a gradual declining trend overall. However, it continues to remain higher than the national target of 6.5 deaths per 1,000 live births (Family Health Development Division, 2023). In 2022, Kelantan reported a perinatal mortality rate of 8.3 per 1,000 live births, surpassing the national average of 8.2 per 1,000. In comparison, the more urbanized and affluent states of Selangor and Johor fared better, recording lower rates of 7.5 and 7.9 per 1,000 live births respectively, likely reflecting their stronger healthcare infrastructure and socioeconomic advantages. Conversely, the East Malaysian states of Sabah and Sarawak, much like Kelantan, grappled with higher perinatal mortality rates of 10.7 and 8.3 per 1,000 live births respectively, owing to challenges in healthcare delivery and geographical barriers (DOSM, 2023b). Interestingly, when benchmarked against global data, Australia reported a slightly higher perinatal mortality rate of 10.1 per 1,000 live births in 2022, exceeding even the concerning figures seen in Kelantan and across Malaysia (AIHW, 2023). This underscores the need for sustained, multipronged efforts to address the complex drivers of perinatal mortality, both within the country and in comparison internationally.

As part of Malaysia’s previous Plan of Action towards achieving Millennium Development Goal (MDG) 4 (2010-2015), one of the strategies was to improve surveillance of Under-five Mortality (U5M), the Ministry of Health has established two separate databases since 2013: the Stillbirth and Under-five Mortality Notification

System (SU5MR System) and the Stillbirth and Under-five Mortality Investigation Form (SU5MR-1/2012). These databases are purposefully created to gather and track data on the mortality rate of children under the age of five including stillbirths (Choo and Manaf, 2020). The U5M reporting system is to report all under-five deaths and stillbirths regardless of place of death, including those from the private sector and deaths outside the hospital. The data on deaths is evaluated and concluded at the district and state levels during monthly meetings focused on perinatal and under-five mortality, which are then reported nationally. The meetings focused on the evaluation of the under-five mortality auditing system's quality by a designated committee. The committee consists of a paediatrician, an obstetrics and gynaecology specialist, a public health physician, a family medicine specialist, and other relevant staff members. The committee's primary duty is to ascertain the factors leading to mortality, categorise them as preventable or non-preventable, and decide on the most suitable course of action (MOH, 2018; HRSA, 2023).

The implementation of the Stillbirth and U5M reporting system aimed to enhance the accuracy of death certification through the utilisation of ICD 10 coding by medical professionals. In cases of deaths that occur outside of hospitals, it is necessary to conduct a verbal autopsy to determine a likely cause of death. This information is then used to assign an appropriate ICD 10 code. Previously, stillbirths were documented and categorised using the PNM formats (PNM 1/97 (amendment 2000) and PNM 2/2012). While stillbirths are not included in the calculation of deaths among children under the age of five, they are considered a component of perinatal deaths. To prevent any repetition in the reporting of stillbirths, the reporting of stillbirths has been incorporated into the new Stillbirth and Under-five Mortality Investigation Form Format (SU5MR-1/2012).

2.2 Perinatal Asphyxia

Perinatal asphyxia accounts for 11% of mortality worldwide in children under the age of five including the perinatal age group, making it the third leading cause of death. According to UNICEF, 80% of deaths in newborns are attributed to three conditions that are preventable and treatable: complications arising from premature birth, deaths related to childbirth (including birth asphyxia), and infections in newborns (UNICEF, 2013). In Malaysia, there is a comparable situation where perinatal asphyxia is the second most common cause of preventable perinatal mortality. In 2022, the percentage of deaths caused by asphyxia was 21.1% (Sutan, 2008). In 2016, the proportion increased to 28.8%, ranking second to prematurity, which accounts for 45.2%. (Family Health Development Division, 2022).

A similar set of findings was also reported by two local studies conducted in Kelantan and Kuala Lumpur. The proportions of perinatal asphyxia that were observed after five years and seven years, respectively, were 21.9% and 22.3% to be exact (Hamzah *et al.*, 2008; Hassan *et al.*, 2013). Global study data from Tanzania and Brazil also showed a similar proportion of perinatal asphyxia (22–30%) in their countries (Schmiegelow *et al.*, 2012; Daripa *et al.*, 2013). This situation hinders our ability to accomplish SDG target 3.2, which aims to eliminate preventable deaths of newborns and children under the age of five.

2.3 Factors Associated with Perinatal Asphyxia

2.3.1 Sociodemographic factors

As far as we know, there have been few studies conducted on the factors linked to perinatal asphyxia in cases of perinatal mortality. While several studies have examined factors related to perinatal or birth asphyxia among live births, research

specifically focused on perinatal asphyxia among perinatal deaths is limited. Hence most of the studies cited in this study were done among live birth or neonatal deaths.

When investigating the phenomenon of perinatal asphyxia, it is essential to take into account the sociodemographic characteristics of the mother. The majority of cases of perinatal asphyxia are reported to be among young mothers between the ages of 20 and 34, according to research conducted in both Brazil and China (Daripa *et al.*, 2013; Yu *et al.*, 2022). The same research conducted by Daripa *et al.* (2013) also indicated that the majority of mothers who delivered babies with perinatal asphyxia were married or in stable unions (48–64%), with the majority of them being housewives.

In a study conducted in Ethiopia, maternal illiteracy was found to be significantly associated with an increased risk of neonatal asphyxia. The adjusted odds ratio for neonatal asphyxia in neonates born to illiterate mothers was six, with a 95% confidence interval ranging from 1.51 to 23.8. This indicates that neonates born to illiterate mothers were six times more likely to experience neonatal asphyxia compared to those born to literate mothers, after adjusting for other factors (Krishnan *et al.*, 2021).

2.3.2 Obstetric-related factors

A selection of studies have reported on the mother's obstetric history, including her antenatal follow up and booking status, underlying comorbidities during pregnancy, parity, and pregnancy status (singleton or multiple gestation) are associated with occurrence of perinatal asphyxia. The prevalence of perinatal asphyxia has been observed to be higher among mothers who did not receive any antenatal care. Antenatal care is defined as the care provided by skilled health-care professionals to pregnant women and adolescent girls to ensure the best possible health for both mother

and baby during pregnancy. Based on a review of the effectiveness of various antenatal care models, the WHO recommends at least four antenatal visits, which increases the likelihood of receiving effective maternal health interventions. However, to reduce perinatal mortality and improve women's care experience, a minimum of eight antenatal visits are recommended (WHO, 2016). Similarly, MOH Malaysia recommends at least eight antenatal visits for multigravida or low-risk mothers (MOH, 2020).

In the Warri Niger Delta region of Nigeria, 60% of asphyxiated cases are caused by unbooked mothers (Ugwu *et al.*, 2012). In India, 58.1% of birth asphyxia cases among full-term babies are the result of mothers who did not receive any antenatal care (Dalal and Bodar, 2013). Meanwhile, in Tanzania, it was discovered that mothers who consistently follow the antenatal visit programme are safeguarded against perinatal mortality (Schmiegelow *et al.*, 2012).

Maternal comorbidities, including hypertension, diabetes, and anaemia, have been significantly associated with an increased risk of neonatal asphyxia. Rattanaprom *et al.* (2023) reported that mothers with any comorbidity had a 1.73-fold higher risk of birth asphyxia (95% CI = 1.47–2.03, *p*-value < 0.001). Additionally, in Southern Ethiopia, neonates born to mothers with anaemia had nearly three times the risk of asphyxia (aOR = 2.99, 95% CI: 1.07–8.35), while those born to mothers with chronic hypertension during pregnancy had almost five times the risk (aOR = 4.9, 95% CI: 1.16–20.7) (Alemu *et al.*, 2019). A case-control study conducted in Uganda involving 210 full-term neonates found that hypertension during pregnancy was significantly associated with an increased risk of neonatal asphyxia. The adjusted odds ratio for asphyxia in neonates born to mothers with hypertension was 3.8, with a 95% confidence interval of 1.49 to 9.5, indicating that these neonates were 3.8 times more

likely to experience asphyxia compared to those born to mothers without hypertension (Krishnan *et al.*, 2021).

Maternal parity is a contributing factor to perinatal asphyxia. Several studies have indicated that nulliparity or primiparity increases the risk of birth asphyxia. In Thailand, the incidence of birth asphyxia was significantly higher in the nulliparous group compared to the multiparous group, with an odds ratio of 1.25 (95% CI = 1.073–1.467, *p*-value = 0.004). This suggests that nulliparous women have a 25% higher risk of their neonates experiencing birth asphyxia compared to multiparous women (Rattanaprom *et al.*, 2023). According to a study by Dalal and Bodar (2013), 57% of cases of full-term birth asphyxia in India are found in mothers who are experiencing their first pregnancy (primigravida). A study conducted in Sao Paolo, Brazil revealed comparable findings, indicating that 54% and 61% of instances of avoidable perinatal asphyxia in the capital and metropolitan area of Sao Paolo, Brazil are observed among primiparous mothers (Daripa *et al.*, 2013). A case-control study conducted in Ethiopia involving 88 neonates with asphyxia and 176 control neonates identified primiparity as an independent risk factor for birth asphyxia, with an adjusted odds ratio of 3.1 (95% CI: 1.51–6.38) (Krishnan *et al.*, 2021).

Another obstetric factor considered in the incidence of perinatal asphyxia is pregnancy status, specifically the presence of multiple fetuses. However, studies have shown that multiple gestation is not significantly associated with the occurrence of perinatal asphyxia. This finding has been consistent across several countries, including Nigeria, Brazil, and China, where the incidence of perinatal asphyxia among mothers with multiple gestations is around 10% or less (Ugwu *et al.*, 2012; Daripa *et al.*, 2013; Yu *et al.*, 2022).

2.3.3 Intrapartum-related factors

Intrapartum factors play a crucial role in the occurrence of perinatal asphyxia. Key factors include the mode of delivery, birth weight of the neonate, gestational age at birth, place of delivery, and the qualifications of the personnel responsible for the delivery. A study by Sendeku *et al.* (2020) found that neonates born via instrumental assisted vaginal delivery had a significantly higher risk of developing perinatal asphyxia, with an odds ratio of 4.04 (95% CI: 2.48–6.60), indicating that these neonates were over four times more likely to experience asphyxia compared to those born via other delivery methods. In China, a study by Yu *et al.* (2022) reported that 46.6% of neonatal asphyxia cases occurred in neonates born via vaginal delivery, and of these, 17.9% were following instrumental vaginal delivery. This highlights the substantial impact of delivery methods on the risk of neonatal asphyxia, underscoring the importance of careful consideration and management of delivery techniques to mitigate this risk.

Babies born with low birth weight (≤ 2500 grams) and those with excessive weight or macrosomia (≥ 4000 grams) are identified as being at heightened risk for perinatal asphyxia, a condition marked by insufficient oxygen supply to the newborn. Rattanaprom *et al.* (2023) conducted a study in Thailand, which revealed significant findings regarding this association. Their investigation revealed notably elevated odds of birth asphyxia in both low-birthweight neonates and those with macrosomia. Specifically, the odds were amplified by 2.31-fold (95% CI = 1.81–2.95, *p*-value <0.001) in neonates with low birth weight and by 1.99-fold (95% CI = 1.32–3.00, *p*-value = 0.001) in those with macrosomia. Moreover, two separate studies conducted in Ethiopia further underscored the correlation between low birth weight and the risk of perinatal asphyxia. According to Alemu *et al.* (2019) and Sendeku *et al.* (2020), the

likelihood of developing asphyxia among low birth weight neonates was found to be considerably higher, with adjusted odds ratios of 3.31 (95% CI: 1.31, 8.37) and 6.52 (95% CI: 4.40, 9.65), respectively. These findings not only substantiate the Thai study but also accentuate the pronounced vulnerability of low birth weight infants to the adverse consequences of perinatal asphyxia.

Several studies have examined the relationship between gestational age at birth and the incidence of perinatal asphyxia. In a comprehensive research conducted in Thailand by Rattanaprom *et al.* (2023), it was determined that the likelihood of asphyxia surged notably at specific gestational age intervals. Late preterm births, ranging from 34 to 36 weeks and six days, exhibited a 1.69-fold increase in the odds of experiencing asphyxia (95% CI=1.43–2.01, *p*-value <0.001), while late-term births, occurring between 41 to 41 weeks and six days, displayed a 1.53-fold elevation in odds (95% CI=1.08–2.16, *p*-value = 0.018). Contrary to these findings, a study conducted in China highlighted a distinct pattern. Yu *et al.* (2022) noted that the majority (74%) of neonatal asphyxia cases occurred within the term gestational age range of 37 to 41 weeks. This observation diverges from the Thai study, suggesting regional variations or differing population characteristics influencing the gestational age-specific risk profiles for perinatal asphyxia. Similarly, investigations conducted in Sao Paolo, Brazil, unveiled subtle patterns in the distribution of perinatal asphyxia cases across gestational age categories. Notably, in the countryside region, 49% of asphyxia cases occurred in infants born at or after 37 weeks of gestation, with extreme prematurity (22 to 27 weeks) contributing to 21% of cases (Daripa *et al.*, 2013). This heterogeneous distribution underscores the multifaceted nature of perinatal asphyxia risk, influenced by diverse geographical and demographic factors.

Additional intrapartum factors contributing to perinatal outcomes include the delivery setting and the attending healthcare provider. A study conducted in Malawi shed light on the impact of delivery location, revealing that women with singleton pregnancies who delivered at home faced a 1.47-fold higher odds of experiencing perinatal death compared to those who delivered in healthcare facilities (McDermott *et al.*, 1996). However, findings from a study in Tanzania contradicted this association, indicating no significant link between home deliveries and perinatal mortality rates (Schmiegelow *et al.*, 2012). Moreover, the expertise of the healthcare provider involved in the delivery process plays a pivotal role. Research conducted by Rattanaprom *et al.* (2023) emphasized the significance of the delivering healthcare provider's specialization. Their study demonstrated a notable increase in the incidence of birth asphyxia when deliveries were conducted by general physicians or residents, as opposed to obstetricians. Specifically, the adjusted odds ratio for birth asphyxia was found to be 1.99 (95% CI=1.58–2.49, *p*-value <0.001) when managed by general physicians or residents. This emphasizes the importance of skilled obstetric care in mitigating the risk of birth asphyxia during delivery, highlighting the critical role of specialized healthcare providers in ensuring optimal perinatal outcomes.

Obstetric events also significantly influence the risk of perinatal asphyxia. The study by Alemu *et al.* (2019) conducted at Dilla University Referral Hospital, Ethiopia, identified several maternal factors associated with perinatal asphyxia, such as anemia during pregnancy, chronic hypertension, and meconium-stained amniotic fluid. The study found that newborns from mothers with chronic hypertension had nearly five times the risk of perinatal asphyxia compared to those without this condition. Additionally, the presence of meconium-stained amniotic fluid was a significant risk factor, increasing the likelihood of perinatal asphyxia by more than threefold (Alemu

et al., 2019). Similarly, the systematic review and meta-analysis by Sendeku *et al.* (2020) suggested that obstetric complications, including prolonged labor and instrumental deliveries, were significant determinants of perinatal asphyxia in Ethiopia and highlighting the critical need for effective obstetric management and monitoring during labor.

The experience and training of healthcare workers are crucial in preventing and managing perinatal asphyxia. Rattanaprom *et al.* (2023) found that hospitals with lower nurse work-hours and those employing combined nursing models (team and primary nursing) demonstrated significantly reduced rates of birth asphyxia. This finding underscores the need for adequate staffing and the importance of continuing education and training for healthcare providers to improve outcomes. The study also emphasized that excellent quality of intrapartum care, characterized by careful monitoring and appropriate interventions like oxygen administration and reduced oxytocin use during non-reassuring fetal status, significantly lowered the risk of birth asphyxia. The study found that higher levels of care quality, particularly in university hospitals, were associated with reduced rates of birth asphyxia.

Quality of care during labor and delivery is another vital factors contributing to the risk of perinatal asphyxia. According to Alemu *et al.* (2019), inadequate prenatal care—specifically fewer than three antenatal visits and a lack of ultrasound checkups—was associated with a higher incidence of perinatal asphyxia. Inadequate intrapartum monitoring, particularly in detecting fetal distress signs such as meconium-stained amniotic fluid or delayed necessary interventions, which increases the risk of asphyxia.

2.4 Conceptual Framework

The conceptual framework shows factors associated with perinatal asphyxia based on the literature review, which includes maternal and intrapartum factors. Factors such as obstetric events, the working experience of the attending healthcare worker (HCW), the shortfall in quality of care, and the quality of intrapartum care and monitoring will not be included as the data are not available or incomplete.

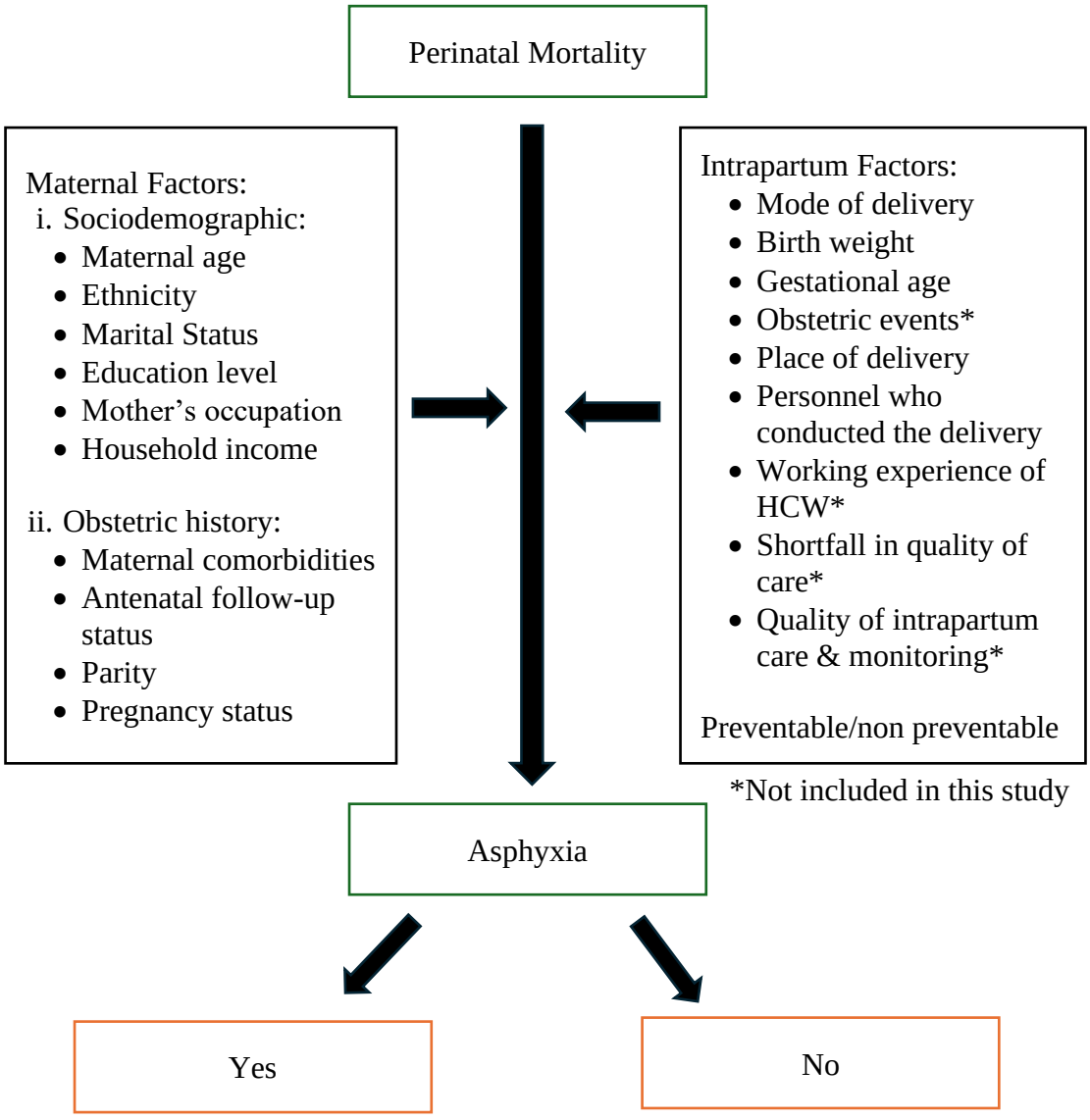

Figure 2-a: Maternal and intrapartum factors associated with perinatal asphyxia among perinatal mortality in Kelantan for years 2020 – 2022.

CHAPTER 3

METHODOLOGY

3.1 Study Type and Design

This was a cross-sectional study based on a retrospective record review of secondary data from the Stillbirth and Under-five Mortality Form (SU5MR-1/2012) that has been obtained from the MCH Unit of the Kelantan State Health Department.

3.2 Study Area

Figure 3-a: Map of Malaysia and Kelantan (figures taken from Abdul Wahab and Ramli (2020)

The study was carried out at the Maternal and Child Health Unit of the Kelantan State Health Department. Kelantan is situated in the northeastern part of Peninsular Malaysia, sharing borders with Thailand to the north, the South China Sea to the northeast, Terengganu to the east, Pahang to the south, and Perak to the west. Kelantan spans an area of 15,040km^2 and is divided into 10 districts: Bachok, Gua Musang, Jeli,

Kota Bharu, Kuala Krai, Machang, Pasir Mas, Pasir Puteh, Tanah Merah, and Tumpat. The state's population in 2020 was 1.79 million people, and its population density was 119 per km^2 (DOSM, 2022).

Kelantan's population is predominantly Malay, with the Malay community making up around 95% of the total population. Aside from the dominant Malay population, Kelantan is also home to small minorities of Chinese, Indians, Thai and indigenous groups such as the Orang Asli. Many residents engage in agriculture, cultivating rice, rubber, and palm oil. Fishing is also a significant activity, especially in coastal areas (Abdul Wahab and Ramli, 2020). The state is famous for its traditional handicrafts, such as batik, *songket* (brocade), and silverware. Many locals are involved in producing and selling these crafts (Kelantan, 2024). Many residents also work in public service roles, given the significant presence of government offices and institutions in the state.

Kelantan had 114 health clinics, 9 government hospitals, 1 university hospital and multiple private clinics and hospitals across its districts (MOH, 2024b, 2024a). The Maternal and Child Health Unit of the Kelantan State Health Department received notices and investigation forms for stillbirths and under-five mortality cases from each of these health facilities.

3.3 Study Duration

The study was conducted from January 2024 to June 2024.

3.4 Study Population

3.4.1 Reference population

All cases of perinatal mortality in Kelantan.

3.4.2 Source population

All cases of perinatal mortality from ten districts were notified to the Kelantan State Health Department from 2020 to 2022.

3.4.3 Sampling Frame

All cases of perinatal mortality from ten districts that were notified to the Kelantan State Health Department from 2020 to 2022 who fulfilled the inclusion and exclusion criteria.

3.5 Inclusion Criteria

All deaths involving the perinatal age group (including stillbirth > 22weeks and birth weight > 500 grams and early neonatal death (from birth until seven days of life), who were notified in the Kelantan Stillbirth and Under-five Mortality Reporting System (SU5MR System) from 2020 until 2022.

3.6 Exclusion Criteria

Missing data of more than 20% of the interested variables from the database.

3.7 Sample Size Estimation

Objective 1:

The sample size was calculated to estimate the proportion of perinatal asphyxia among perinatal mortality in Kelantan by using a single proportion formula (Arifin, 2013). A sample size of 397 was estimated to be sufficient to address this first objective, including an additional 20% possibility of missing data (95% confidence, $Z\alpha = 1.96$ and the precision, $d = 0.05$). P is the value of prevalence of perinatal asphyxia among

perinatal mortality. The prevalence of perinatal asphyxia among perinatal mortality was 28.8% (Family Health Development Division, 2022).

Single proportion formula

$$n = \left(\frac{Z_{\alpha}}{d} \right)^2 * P(1 - P)$$

$$\left(\frac{1.96}{0.05} \right)^2 \text{ x } 0.29 \text{ (1-0.29)}$$

$$= 1536.64 \text{ x } 0.29 \text{ (1-0.29)}$$

$$= \frac{(1536.64 \text{ x } 0.21)}{(1 - 0.2)} \longrightarrow \text{20\% possibility of missing data}$$

$$= \mathbf{397}$$

Objective 2:

The sample size was calculated by using an independent two-proportion comparison formula in PS Software (dichotomous). The power of the study was set at 80% with α=0.05. The calculation will be applied to each variable with 20% additional as a possibility of missing data.

Table 3-1: Sample size calculation for factors associated with perinatal asphyxia among perinatal mortality in Kelantan for 2020 to 2022.

Variables	**P_1**	**P_0***	**m**	**n**	**N = (n x (m+1) / (1-0.2)**	**Literature Review***
Parity (Primiparous)	0.60	0.36	2	50	188	Rattanaprom *et al.* (2023)
Occupation (Housewife)	0.50	0.30	2	69	259	Daripa *et al.* (2013)
Marital Status (Married)	0.70	0.46	1	65	163	Daripa *et al.* (2013)
Mode of Delivery (Vaginal Delivery)	0.70	0.46	1	65	163	Daripa *et al.* (2013)

P_0 = proportion of non-exposed who had perinatal asphyxia

P_1 = estimated proportion of exposed who had perinatal asphyxia

m = ratio non-exposed / Exposed

After considering all the calculations, the sample was chosen using a single proportion calculation method, which determined the minimum number of samples needed to achieve the study's objectives. The sample size required to perform these analyses was 317 respondents. Therefore, the total number of respondents included in the sample after accounting for a 20% drop-out rate was 397.

3.8 Sampling Method

In the dataset on perinatal mortality in Kelantan, there were 866 deaths that occurred between the year 2020 and 2022. After applying the exclusion criteria, we were able to collect 397 samples for this study by using simple random sampling method. This sampling process was conducted using Microsoft Excel. Initially, all cases were listed in the proforma checklist. The =RAND() function was then used to generate a random number for each cases. Subsequently, all cases were sorted based on the random number column, effectively shuffling the data randomly. The top 397 cases were then selected from the sorted list. This approach ensured that each cases had an equal chance of being included in the study.

3.9 Operational Definition

1. Perinatal Mortality

   All mortality cases occurred in the perinatal period and with birth weight equal to or more than 500 grams. The perinatal period was defined as the period after 22 weeks of pregnancy, birth and the first seven days of life (MOH, 2018).

2. Perinatal Asphyxia

   Perinatal asphyxia refers to the condition where the fetus experiences insufficient blood flow or gas exchange during, before or after the birth process (Gillam-Krakauer and Gowen Jr, 2022).

In this study, perinatal asphyxia referred to the subclassification of ICD-10 classification that was recorded as 'HIE/birth asphyxia/neonatal encephalopathy' in the softcopy template of the Stillbirth and Under-five Mortality Investigation Form (SU5MR-1/2012).

3. Preventable Death

   All deaths that can be prevented through medical (such as delayed referral or delayed treatment) and non-medical interventions (such as public health policies that address social, patient or family factors) (MOH, 2017).

4. Non preventable Death

   All deaths caused by life limiting diseases such as lethal congenital malformation, inborn error of metabolism, or severe inoperable congenital heart disease (MOH, 2017).

5. Maternal Age

   In this study, maternal age has been categorized into four categories: adolescent mother, mother aged 20 – 35 years old, advanced maternal age mother and very advanced maternal age mother.

   The definition of adolescent mother was referred to pregnant women aged 10 – 19 years old (WHO, 2023a). While advanced maternal age mother was referred to those aged 36 to 47 years old and very advanced maternal age refers to those aged > 48 years old (Attali and Yogev, 2021).

6. Household Income

   In Malaysia, household income has been categorized into three primary groups: the Bottom 40% (B40), the Middle 40% (M40), and the Top 20% (T20). The B40 household group (the lowest-earning group) pertains to those earning less than RM5,250 per month. Meanwhile, households earning between RM5,250 to

RM11,819 were classified as M40 households (middle-earning group), while T20 referred to those earning RM11,820 and above (highest-earning group) (DOSM, 2023a).

However, for this study, due to the limitation of secondary data available, household income was classified into three categories: the lowest-earning group, which was those with income less than RM3000, the middle-earning group those with income between RM3000 to RM6999 and the highest-earning group was those with income of RM7000 and above.

7. Antenatal follow-up status

   In our study, we followed the WHO and MOH's recommendations as documented in the Stillbirth and Under-five Mortality Investigation Form (SU5MR-1/2012) and classified the cases into two categories: adequate antenatal follow-up status, in which the mothers received at least eight antenatal check-ups, and inadequate follow-up or unbooked status, in which the mothers received no antenatal check-ups or had fewer than eight visits.

8. Birth weight

   The cases' birth weight was classified into three categories: normal birth weight, low birth weight, and macrosomic. The range for normal birth weight is between 2500 grams and 4000 grams. Low birth weights were defined as infants with a birth weight below 2500 grams. Macrosomic refers to infants who have a birth weight exceeding 4000 grams (Kaur *et al.*, 2019).

9. Gestational age

   The gestational age at birth for all the cases was categorised into three categories. Term gestation refers to those who were born at a gestational age of 37 weeks or more. Late preterm are those born between 34 and 36 weeks, while

moderate to extreme preterm refers to those born at or before 33 weeks (Muglia and Katz, 2010; MOH, 2023).

10. Place of delivery

In this study, the place of delivery has been categorised into 1) hospitals with specialists, including government hospitals with specialists and university hospitals; 2) hospitals without specialists; 3) private hospitals and maternity homes; 4) health clinics; and 5) delivery outside of health facility (which includes home delivery, en route or during transportation, and others).

3.10 Data Collection Method and Research Tools

This study used secondary data collection. The primary investigator conducted the data collection, sourcing it from the Stillbirth and Under-five Mortality Notification System (SU5MR System) (Appendix A) and the Stillbirth and Under-five Mortality Investigation Form (SU5MR-1/2012) (Appendix B), both of which were provided by the Maternal and Child Health Unit from the Kelantan State Health Department. The SU5MR System was established by the Ministry of Health, Malaysia in 2013 to report under-five deaths, including those from the private sector and outside hospitals. All deaths are investigated, identified, and classified as preventable or otherwise, and under-five deaths (live births until less than five years old) and stillbirths are reported to the District Health Office by filling out the corresponding notification form U5MR-N within 24 hours of the death. The forms are then sent to the Kelantan State Health Department within 24 hours and verified before being reported to the Ministry of Health within the same time frame. Hospitals or health clinics manually investigate and record all deaths on the Stillbirth and Under-five Mortality Investigation Form (SU5MR-1/2012). The form is sent to the District Health Office within one week of the death and