Assessing Possible Risk Factors Contributing to Maternal Morbidity: A Systematic Review of the Relative Link Between Pre-Eclampsia, Traumatic/Acquired Brain Injuries and Epilepsy in Maternity

Abstract

The journey to motherhood is a fulfilling one incorporating compassion and love for the child. However, this optimism is faced with high uncertainty for the mother and child considering the escalating maternal morbidity during maternity. This dissertation aimed to analyse potential risk factors associated with maternal morbidity by conducting a systematic review of the relative link between pre-eclampsia, traumatic/acquired brain injuries and epilepsy in pregnancy outcomes. Pre-eclampsia is a hypertensive disorder relatively common among those who are pregnant; it is one of the leading causes of maternal mortality and morbidity. Similarly, traumatic and acquired brain injuries (TBIs) and epilepsy can lead to poor pregnancy outcomes such as pre-term delivery and cortical injury to the infant, and death of the mother. Data from Medline, Cinahl, and Cochrane databases were sourced for this review. Published literature not older than five years was critically reviewed. The eligibility criteria, review methods and inclusion criteria were established before commencing the evaluation of published data. The outcome of the systematic review was the identification of potential maternal morbidity risk factors associated with pre-eclampsia, traumatic and acquired brain injuries and epilepsy in pregnant women. The findings of this study indicate that there is an established association between pre-eclampsia and TBI and/or epilepsy in pregnant mothers; however, further research is required to determine the level of causality between the factors and adverse pregnancy outcomes. The systematic review of existing literature also provides an opportunity to develop comprehensive strategies and guidances to reduce maternal morbidity related to pre-eclampsia, traumatic / acquired brain injuries and epilepsy.

Table of Contents

List of Figures & Tables

Chapter 1. Introduction

Parenthood is an incredible experience that encompasses love, hardship, and newfound purpose. It is both awe-inspiring and demanding, and many of the accompanying physical symptoms are shared between all expecting mother's journeys. In particular, pre-eclampsia, traumatic and acquired brain injuries, and epilepsy can be life-threatening complications that result from an improperly monitored pregnancy (Nyfløt et al., 2017). Menon and Irving (2022) suggested that preeclampsia is a multisystem disorder that plays a role in maternal complications during pregnancy and postpartum. The impacts of preeclampsia during pregnancy can be severe and even fatal if not properly treated.

Maternal morbidity is an important and growing field of study and one that needs more research and attention. Maternal morbidity is a term used to describe physical and psychological problems associated with pregnancy, childbirth, and the postpartum period (Leonard, Main & Carmichael, 2019). The UK has seen a consistent trend of increasing maternal morbidity over time despite significant advances in terms of perinatal and obstetric care. According to Public Health England, since 2006-2012 there has been a 54% increase in maternal mortality rates and a 131% increase in the number of severe morbidity cases (Knight et al., 2020).

Traumatic brain injury is a critical factor leading to mortality during pregnancy (Vigil et al., 2020). Unfortunately, it can affect pregnant women and if not detected earlier, can prove lethal. Tran et al. (2019) cite that injuries suffered by pregnant women are not minor, and should be treated with extreme care.

In addition to head injuries caused by conditions such as preeclampsia, post-traumatic epilepsy can also be a complication arising from brain injuries (Tran et al., 2019). Epilepsy is a common condition that involves occasional seizures which cause a sudden burst of electrical activity in the brain, temporarily affecting how the brain functions. Possible symptoms may include uncontrolled shaking of the body, stiffness, strange smells and tastes, tingling in the arms or legs, collapsing or losing consciousness. Generally, epileptic seizures can be caused by damage to the brain due to stroke, brain tumour, drug or alcohol abuse, brain infections and birth complications that included poor oxygenation (Shoopala & Hall, 2019). With certain seizure effects, such as a lack of control, related injuries to the head may also arise, leading to more serious complications. According to Menon and Irving (2022), there are three major types of seizures that can arise from epilepsy. Therefore, the chances of a pregnant woman with a mild or severe head injury being identified with epilepsy are significant.

To explore the relationships between pre-eclampsia, traumatic/acquired brain injuries, and epilepsy and maternal morbidity, this dissertation will undertake a systematic review of the available literature in this area. The systematic review will focus on identifying any associations between the conditions and maternal morbidity, particularly any biological and/or physiological mechanisms that might explain the link. This dissertation will examine native studies in the UK as well as international studies from multiple perspectives such as medical, nursing, and public health to gain a more comprehensive understanding of what is known about the possible risk factors relating to maternal morbidity.

Chapter 2. Literature Review

2.1 Introduction

This literature review examines previous studies on the impact of preeclampsia and the further medical complications it can lead to including the long-term effects imposed on motherhood. To identify relevant articles, a comprehensive search of the available literature was conducted.

2.2 Search description

The search was conducted on credible databases including CINAHL Plus, Cochrane, and MEDLINE. The search was conducted using keywords such as "pre-eclampsia", "traumatic/acquired brain injuries", "epilepsy", "maternity", and "maternal morbidity". The search was limited to articles published in the English language over the last ten years (2013-2023). This allowed attaining recent evidence concerning the topic. Additionally, the search was restricted to articles involving women of childbearing age. The inclusion criteria for this systematic review was thus an article that studied the association between pre-eclampsia, traumatic/acquired brain injuries and epilepsy during pregnancy. Exclusion criteria included any article that did not involve human subjects, was not in the English language, did not involve women of childbearing age, and did not focus on the study topic. The search yielded 822 results. These articles were then screened for relevance and non-relevant articles were excluded. After the screening process, a total of 21 articles were selected for this systematic review as shown in Figure 1.0 below.

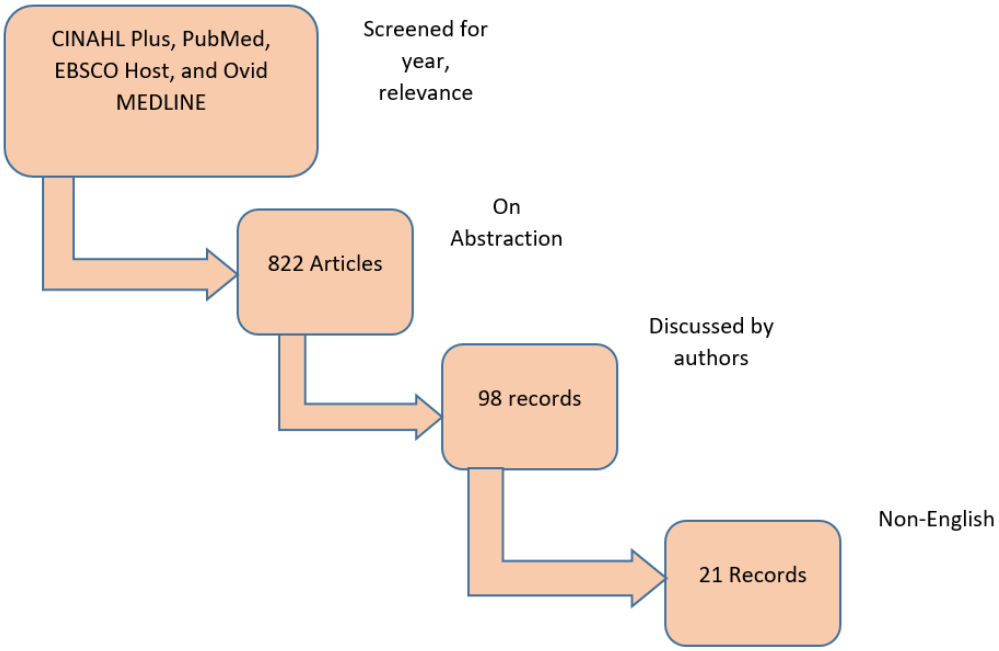

Figure 1.0 Screening for Relevant Articles

All of the selected articles were then evaluated in-depth to assess the study topic. The results of this systematic review will be discussed in the following sections.

2.3 Conceptual/theoretical framework

Traumatic-acquired brain injury has been linked to several factors. Physiologically, pre-eclampsia, traumatic/acquired brain injuries and epilepsy during pregnancy can result from a variety of factors, including maternal health conditions, genetic factors, infections, and nutritional deficiencies. Research has also suggested that there may be a correlation between pre-eclampsia, traumatic/acquired brain injuries and epilepsy, and other conditions related to hypertension, such as gestational diabetes, pre-existing medical conditions and large-for-gestational age babies (Black et al., 2015). In terms of environmental factors, research has indicated that risk factors for maternal morbidity may be connected to stressful and complex

categories, such as domestic abuse, certain lifestyle characteristics, and the presence of certain psychological stressors (Hirshberg& Srinivas, 2017). For instance, some studies have suggested that distress, prior trauma, and serious mental health issues in pregnant women could increase the risk of pre-eclampsia, traumatic/acquired brain injuries and epilepsy (Darlan, 2021; Gambhir et al., 2019). Thus, when evaluating traumatic brain injury, it is critical to consider these factors owing to their role in these factors.

2.4 Review of research

2.4.1 Preeclampsia, traumatic or acquired brain injury and epilepsy

Tantillo et al. (2020) found that women who experience pregnancy-related complications, including pre-eclampsia and eclampsia, are at a higher risk of postpartum readmission for seizures and epilepsy. Similarly, Bergman et al. (2018) found that biomarkers such as plasma concentration associated with brain injury were elevated in women who later developed pre-eclampsia. This suggests that there may be a correlation between pre-eclampsia and brain injury. Han et al. (2018) examined the changes in the expression of aquaporins (AQP4 and AQP9) in the hippocampus following eclampsia-related seizures. The authors found that the expression of AQP4 and AQP9 was significantly increased, suggesting that there may be a role for these proteins in the development of brain injury in women with eclampsia.

Additionally, Danielsson et al. (2018) found that the number of pregnancies was a significant risk factor for complications in pregnant women with epilepsy. This highlights the importance of appropriate management and monitoring during pregnancy for women with epilepsy. Al Bizri et al. (2021) in a multi-centre studyfocused on the timing of term elective cesarean section and adverse neonatal outcomes. The findings indicated that uncomplicated elective planned

caesarean sections accounted for 25% of all deliveries in the sampled participants (28,997 women) and 9.7% of all deliveries from 2001-2017 in Lebanon. These outcomes were significant considering the large sample size used (28,997 women). This study is relevant to the overall topic of maternal morbidity and its impact on neonatal outcomes as it showed few instances of adverse neonatal outcomes (less than a third of sampled participants).

Traumatic brain injury is another form of neurological manifestation commonly seen in postpartum women due to physical trauma sustained before or during delivery (Aria Jazdarehee et al., 2022). Bergman et al. (2018) suggest that acute changes taking place in plasma concentrations of neurofilament light chain (NfL) Tau S100B, NSE may also occur before diagnosis suggesting novel ways cerebral biomarkers can be used for diagnosing TBIs associated with pre-eclamptic seizures.

Increased risk of seizures and epilepsy in women with pre-eclampsia is also a critical concern. Tantillo et al. (2020) found that women with pre-eclampsia were more likely to be readmitted for seizures and epilepsy after childbirth than those without the condition. Similarly, Han et al. (2018) found that women with pre-eclampsia-like seizures had changes in the expression of certain proteins in their hippocampus, which may be involved in the development of epilepsy. Another common theme in the literature is the potential impact of traumatic or acquired brain injury on maternal morbidity and mortality. Al Bizri et al. (2021) found complications during cesarean sections performed before 39 weeks of gestation were associated with an increased risk of adverse neonatal outcomes, including traumatic brain injury.

Duffy et al. (2019) explored the perspectives of women with lived experience of pre-eclampsia and found that they identified neurological complications, such as stroke and brain injury, as significant concerns.Epilepsy is also a significant concern, with several studies exploring the

impact of this condition on maternal health during pregnancy and childbirth. Danielsson et al. (2018) found that women with epilepsy had an increased risk of certain complications during pregnancy, including pre-eclampsia, and that this risk was higher in women who had given birth before. Bergman et al. (2018) identified potential biomarkers in the blood that may be associated with the development of epilepsy in women with pre-eclampsia.

Most studies report how excess morbidities can follow up on mothers if they experience any one issue during birth (Wosenu et al., 2018; Kho and Abdullah, 2018). Hence, evidence suggests that women's health should remain paramount throughout their pregnancy particularly when the primary caregiver gets an indication that either the mother, foetus or both are at risk due to increased chance of generating secondary issues like brain injury and pre-eclampsia. It appears paramount for healthcare workers especially those managing emergency-related problems related to born babies and mothers must remain vigilant so active management strategies are applied promptly.

Lolk et al. (2022) conducted a Danish nationwide cohort study to analyse the impact of perinatal adversities such as pre-eclampsia and TBI/ABI on the risk of developing epilepsy in mothers. The study used data from administrative registries including the Danish National Register of Patients from 1978 to 2016 to identify 30,566 individuals with epilepsy and 315,780 controls who did not have epilepsy. Covariates included pregnancy information, which accounted for 7.1% of pre-eclampsia cases and 40.3% of TBI/ABI cases among the sample population. Statistical analyses were performed to assess the associations between perinatal adversities and epilepsy. The findings revealed that pre-eclampsia was associated with a risk of developing epilepsy, while TBI/ABI only had a marginal association with epilepsy.

Farnaaz et al. (2022) conducted a study on maternal and fetal outcomes related to eclampsia in a tertiary care hospital. The study used a prospective observational design on a sample size of 225 pregnant women aged 15–40 years admitted to the hospital with eclampsia during the study period which was six months. Data were collected using questionnaires and analysed using descriptive statistical analysis techniques. The findings showed that 28% of patients had a relapse of seizures after discharge from the hospital and the mode of delivery in 79% of eclamptic women was a caesarean section. Preterm births were observed in 49% of the cases and babies born small for gestational age were found in 35% of eclamptic pregnancies. These findings imply that eclampsia significantly affected foetal outcomes and contributed to high mortality and morbidity. Therefore, this attribute is a critical concern considering the impact on the quality of life not only for the mother but for the children.

Adlam (2021) studied early onset pre-eclampsia with severe features in 146 pregnant women admitted to Tygerberg Hospital from 2017-2019. A prospective observational design was used for data collection over two years and descriptive statistics were employed for data analysis by dividing the sample into two groups based on birthweight: 1000–1800 g versus 1800–2500 g. Results revealed that severe maternal complications such as seizures occurred more frequently in those with low birth weight babies compared to those with higher birth weight babies (27% versus 8%). The newborns also had a greater risk of morbidity or mortality, while 74% of mothers in the 1000–1800 g group were known to have pre-eclampsia before delivery compared with 28% in the other group.

Johnston et al. (2020) studied maternal collapses during pregnancy or delivery using a guideline based on reviews of evidence in order to inform clinical practices. The evidence presented supported both preventive measures such as increased vigilance in pregnant women at risk for

eclampsia. Evidence also indicated that in some instances, prophylactic magnesium sulphate can be useful for inducing, but complications arise where there is preeclampsia or an increased risk thereof. Furthermore, it was also recommended that women with previous birth complications should receive frequent clinical assessment throughout labour due to the increased risk of pre-eclampsia which can lead to seizures requiring urgent clinical interventions and multidisciplinary management due to risk for neurological outcomes such as epilepsy after delivery or antenatal insults or interventions during delivery or postpartum periods.

Miller et al. (2022) provide an overview of the pathophysiology of cerebrovascular changes during preeclampsia and eclampsia, focusing primarily on causing mechanisms, natural history and consequences for long-term neurological outcomes. Evidence presented in this paper suggests that cerebral hypoperfusion caused by high systemic blood pressure may contribute to seizures complications seen during delivery or postpartum periods from preeclamptic insults that increase the risk for long-term neurological outcomes such as epilepsy in adults due to maternal insults or interventions during delivery or postpartum periods due to pre-eclampsia and eclampsia related complications.

Baschat et al. (2018)assess the association between maternal blood-pressure trends and pre-eclampsia in women who received first-trimester aspirin prophylaxis. The study was conducted as a prospective study involving a total sample of 2,123 women who were recruited in the first trimester of pregnancy and followed up until delivery. The women were divided into three groups based on the timing of first-trimester aspirin prophylaxis: initiation in the first trimester (n = 572), delayed initiation after the first trimester (n = 1,388), and no aspirin prophylaxis (n = 163). The authors used generalized estimating equations (GEE) to analyse the data and to assess the association between blood pressure trends and pre-eclampsia.

The results showed that women who received aspirin prophylaxis in the first trimester had a lower risk of pre-eclampsia compared to those with delayed initiation or no aspirin prophylaxis. The authors concluded that initiation of first-trimester aspirin prophylaxis is associated with a decreased risk of pre-eclampsia and that women who receive early initiation have improved blood pressure trends throughout pregnancy compared to those who initiate aspirin prophylaxis after the first trimester, or those who did not receive any aspirin prophylaxis.

2.4.2 Pre-eclampsia and maternal complications

Several studies sources suggest a definitive connection between pre-eclampsia and maternal morbidity, which can even be prevented in certain cases. For example, in the investigation by MacDonald et al. (2019), pre-eclampsia was found to have caused more than a third of all severe maternal morbidity instances among the 50 participants employed in the study. This emphasises the importance of identifying and diagnosing pre-eclampsia early, given that it poses such a large risk to maternal health. Additionally, the findings from Hayes-Ryan et al. (2019) and Cerdeira et al. (2018) suggest that placental growth factor (PGF) could potentially be used to assist with pre-eclampsia diagnosis and ultimately with decreasing maternal morbidity. Similarly, a connection was found between epilepsy in maternity and severe maternal morbidities. Ndwiga et al. (2020) suggest that pregnant women with these epileptic conditions are predisposed to severe maternal complications and high mortality rates for both mothers and babies.

These findings point to the need for improved recognition and clinical management of these conditions in order to improve maternal and foetal outcomes. Meanwhile, Maher et al. (2019) did not explicitly identify a link between pre-eclampsia and neurodevelopmental outcomes, but it appears that inflammation may have some role in mediating adverse effects on offspring development as suppositions by the authors. This review by Maher et al. (2019) highlights gaps

in this knowledge area, which should be explored further through more research into the pathophysiology underlying pre-eclampsia. In the MacDonald et al. (2019) study, it was found that out of all cases of pre-eclampsia, 25% resulted in severe maternal morbidity, with the main preventable factors being gestational hypertension, the long second stage of labour and gestational diabetes. All these are pre-existing conditions or known risk factors for pre-eclampsia and subsequently for morbidity.

Hayes-Ryan et al. (2019) examined the potential to use placental growth factor levels to better predict pre-eclampsia in pregnant women, in order to reduce maternal morbidity; however, the results were inconclusive due to the use of a stepped wedge cluster randomized controlled trial. This highlights the potential need for more research to better identify those at risk from pre-eclampsia and its associated risks. Ndwiga et al. (2020) looked at a cohort in Kenya, whereby 48% of women experienced either pre-eclampsia or eclampsia and there was an identified association with poor economic status as a risk factor. This suggests that education to support better economic circumstances may help to reduce the incidences of pre-eclampsia and corresponding risks. Cerdeira et al's. (2018) article discussed the evidence for angiogenic factors as predictors of the severity of pre-eclampsia, however, found their use could not be recommended for clinical implementation due to a lack of robust clinical evidence. The Maher et al. (2019) article discusses neurological implications for infants exposed to pre-eclampsia during uterine development, again highlighting that women with high-risk factors need increased antenatal care and monitoring in order to reduce any potential risks to infants from pre-eclampsia exposure.

Dimitriadis et al. (2023) reviewed evidence from a wide range of epidemiological and clinical studies that investigated factors related to pre-eclampsia occurrence, risk factors, diagnosis,

management, complications and prognosis. The methodology of the study included a literature search using the keywords 'pre-eclampsia' on Medline and Embase databases based on predetermined eligibility criteria. The results of the literature search revealed 277 articles; out of which eight studies were included in the review. The findings suggested that prior conditions such as obesity and hypertension are associated with an increased risk of pre-eclampsia, confirming already established risk factors. The methodology adopted by Dimitriadis et al., (2023) appears to be reliable; however, due to the short timeframe to explore a wide range of articles, it is difficult to assess their accuracy. Besides, the smaller sample size implies that the findings could not be generalized to a wider context. However, the study provides sufficient literature on the topic of interest.

Valencia-Ortega et al. (2020) aimed to review evidence for immune tolerance between mother and fetus in pregnancies affected by pre-eclampsia. The authors collected from articles published since 2001 from Embase, Medline, Scopus and Web of Science databases using "pre-eclampsia" as keyword search terms. The results revealed a total of 219 articles that were assessed for eligibility according to predetermined selection criteria; 17 articles were included in the final review. The findings demonstrated that several immunological changes related to pre-eclampsia may play an important role in the development of maternal immune tolerance. The results are reliable due to the use of evidence-based databases for articles search and the large sample sizes used by each study (>700 participants).

Shoopala et al. (2019) sought to re-evaluate the impact of expectant management of early onset pre-eclampsia on maternal complications such as abruption placentae and other maternal outcomes in women from ethnic minorities susceptible to preeclampsia. To this end, Shoopala et al. (2019) conducted comprehensive literature involving pre-eclampsia management published

until June 2019. They included 15 studies consisting of three RCTs with 2158 participants with pre-eclampsia. The findings revealed that expectant management was not associated with perinatal mortality, abruption placentae or maternal death but associated with increased incidence of emergent caesarean delivery and low Apgar scores at five minutes. The methodology used in this article appears to be appropriate however additional studies may need to be included in order to understand the impact of expectant management better.

Tochio et al. (2019) study investigated whether pre-eclampsia without proteinuria leads to different pregnancy outcomes than pre-eclampsia with proteinuria. This study identified ten studies for review through a systematic search on multiple databases including PubMed and Embase released before 2018 with the keywords "pre-eclampsia" or "preeclampsia" or "pregnancy-induced hypertension" which were used as search terms. The sample size ranged from 20 to 3200 women who developed pre-eclampsia during pregnancy; out of these, only four studies reported sufficient data on outcomes if there was no proteinuria. The findings revealed that pre-eclampsia without proteinuria is associated with comparable perinatal outcomes and risk levels as those with proteinuria that require treatment on an analogous basis. The study included a large sample size which justifies its reliability. Although the articles included were fewer, they were recent and could provide good information concerning the topic of study.

Similarly, Bijl et al. (2022) described patients' journeys during and after a pregnancy complicated by pre-eclampsia by conducting an observational study based on a large healthcare system database comprising 13784 women diagnosed with pre-eclampsia between 2011–2016 at or shortly before delivery. The study excluded those diagnosed before 20 weeks gestation or after 42 weeks gestation, due to incomplete data on diagnosis timing. This research employed descriptive analysis encompassing frequencies for categorical variables They found that the

overall prevalence of postpartum psychological concerns up to six months postpartum varied greatly between those who had mild disease and with severe disease based on their criteria for mild/severe scenarios; mental health support utilization was highest again amongst those who had more severe complications due to pre-eclampsia up to two years after delivery. The findings present reasonable evidence which suggests that there is an increased likelihood for maternal psychological problems and subsequent mental health services utilization following diagnosis with pre-eclampsia during pregnancy regardless of when they occur and can continue up to two years post-delivery. These results are reliable due to the large sample size used.

2.4.3 Traumatic brain injury in non-obstetric mortality

The literature review of traumatic brain injuries in pregnant women has highlighted the importance of a multidisciplinary team approach to ensure that the safety of both mother and baby is maximised. Evidence suggests that early detection is vital in order to prevent the condition from manifesting, leading to subsequent risks including death. Vigil et al. (2020) suggest that pharmacological treatment may be beneficial in preventing further head injuries, haemorrhage and neuronal damage, while Spaite et al. (2019) suggest that standardised protocols are needed throughout hospitalisation following traumatic brain injury to maximise patient survival.

Kho and Abdullah (2018) explored the particular risk factors pregnant mothers face; due to their anatomy potentially making their recovery more complex. Additionally, Wu et al. (2017) found that long-term physical issues such as kidney damage may have implications for the health of the mother beyond just the time of delivery but down the line. Further, Safdari et al., (2018) argued that further research is needed to assess the long-term implications for foetuses following secondary head trauma from a motor vehicle accident and Darlan et al. (2021) present a follow-

up algorithm for cases where Traumatic Brain Injury (TBI) is suspected in pregnant mothers. These findings stress the need for medical professionals to be able to identify and respond appropriately by implementing an appropriate algorithm.

Al Fauzi et al., (2023) investigated the prevalence and severity of TBI from a systematic review of existing data from eight studies with sample sizes ranging from 30 to 1074 subjects. In their findings, the authors reported that TBI during pregnancy affects roughly 2-10% of pregnant women, with lower prevalence in low-income countries and higher prevalence in middle- and high-income countries. This difference could be partly attributed to differences in access to medical care and resources. In terms of severity, the most commonly reported TBI was mild (53-84%). However, moderate to severe head injuries occurred in 10-15% of cases. Based on these findings, the authors concluded that TBI during pregnancy is an important public health problem that is associated with significant morbidity and mortality. They further suggested that physicians should have a better understanding of TBI during pregnancy and focus on preventive measures such as increased use of safety devices and protective gear for women at risk of falls.

Menon and Irving (2022) focused on trauma during pregnancy with an emphasis on clinical management and outcomes. Using a retrospective medical records analysis of over 890 patients at three trauma centres in the United States, they reported that blunt abdominal trauma was commonly associated with head injuries (42%) followed by extremity injuries (37%). In terms of clinical management, telemedicine was recommended for minor trauma cases; however, for severe cases with high mortality risk, physicians relied on invasive procedures. The authors also reported that in most cases the outcome was favourable despite any potential complications or maternal fatality due to severe trauma. Consequently, they concluded that proper treatment is essential for reducing maternal mortality from traumatic injuries during pregnancy.

Similarly, Ormesher et al. (2019) critically examine the possible risk factors contributing to pre-eclampsia, traumatic/acquired brain injuries and epilepsy in maternity. The study particularly focuses on the relationship between pre-pregnancy cardiac dysfunction and pre-eclampsia. The authors conducted a systematic review of the literature over a period of 10 years (2008-2018) to identify relevant studies and data related to this topic. The study used a meta-analysis approach to synthesise the retrieved data, which included a total of 95 studies. The authors used several inclusion criteria to select the studies they analysed, such as the inclusion of pregnant women, pre-eclampsia and cardiac dysfunction. The primary outcome measure used was the prevalence of pre-eclampsia and its association with pre-pregnancy cardiac dysfunction. The authors also conducted an analysis to examine the risk of pre-eclampsia among women with cardiac dysfunction and those without.

The study sample consisted of 5,181 pregnant women, and the majority of the studies included were prospective cohort studies (88.4%). The authors found that the overall prevalence of pre-eclampsia was 10.6% among women with pre-pregnancy cardiac dysfunction, compared to 4% for women without cardiac dysfunction. The study also found that women with cardiac dysfunction were more likely to develop pre-eclampsia (OR = 2.63; 95% CI 1.47-4.71). The study also included a number of other risk factors that may be associated with pre-eclampsia, such as ethnicity, obesity and diabetes. However, the authors concluded that the evidence was not sufficient to confirm a causal relationship between these risk factors and pre-eclampsia.

Thus, this study provides valuable insights into the relationship between pre-eclampsia, traumatic/acquired brain injuries and epilepsy in maternity. The study employed appropriate methods to analyse the existing data and evidence, with the authors conducting a systematic review of literature, conducting a meta-analysis to synthesise the retrieved data and using a large

sample size. Although the study did not find sufficient evidence to confirm a causal relationship between other risk factors and pre-eclampsia, it does provide strong evidence that pre-pregnancy cardiac dysfunction is a risk factor for pre-eclampsia.

Singh et al., (2020) investigated acute head injury during pregnancy with an observational case series study consisting of 20 subjects from two hospitals in India. Their results showed that 36% had mildly impaired consciousness at admission but all subjects recovered at discharge after mild management such as speech therapy for long time tracheostomy use whereas 56% required moderate management consisting of fluid infusion medications for controlling convulsions, hypertensive episodes etc., 7% had severe management requiring tracheostomy and long term ventilator support along with medications, 5% expired due to severe TBI with chest infection at the second trimester. They concluded that acute head injury can significantly affect the progress of the entire pregnancy but most times it can still be managed successfully if interventions are conducted timely based on adequate information regarding the exact cause along with professional guidance throughout the entire duration of pregnancy.

2.4.4 Maternal complications before and during childbirth

Several studies have focused on maternal complications during and after childbirth and identified the common themes regarding risk factors associated with this adverse health condition. An assessment of the evidence was undertaken in order to see if there is a link between pre-eclampsia or trauma-acquired brain injuries and epilepsy, and maternal morbidity. The research found that maternal haemoglobin concentrations across pregnancy could be associated with undesirable outcomes for both mothers and their children (Young et al., 2019). It was also seen that maternal pregnancies had increased complications in those with polycystic ovary syndrome (Bahri Khomami et al., 2019). Further, head injuries in infants and toddlers could lead to seizures

and subdural haemorrhage (Högberg et al., 2018; Narisawa et al., 2022; Giovanna Marchini et al., 2020). Postpartum haemorrhage was also linked to risk factors including preterm delivery, primary caesarean section, younger gestational age at delivery, and anaemia (Bazirete et al., 2022).

When assessing pre-eclampsia, there is evidence that this can be a risk factor when it comes to both maternal health and prematurity of the foetus. Specifically, pre-eclampsia can cause hypertension in the pregnant woman which is attributed to foetal growth restriction and higher risk for stillbirths, and fetal death (Young et al., 2019). Young et al. (2019) opine that pre-eclampsia may be managed using magnesium sulphate therapy or antihypertensive drugs.

When looking at acquired brain injury there is evidence that this can cause a range of symptoms ranging from cognitive impairments, seizures and behavioural problems (Högberg et al., 2018; Narisawa et al., 2022; Giovanna Marchini et al., 2020). Furthermore, it has been shown that specific types of trauma or injury can cause permanent damage to the brain which can have long-term impacts on both the mother's health and the development of her baby (Högberg et al., 2018). Thus, it is important for healthcare professionals to consider both the short-term and long-term impacts of acquired brain injury when caring for expectant mothers.

Regarding epilepsy, research has suggested that it can increase the risk of miscarriages during early pregnancy (Bahri Khomami et al., 2019). However, further research is needed to understand what other complications may be associated with epilepsy in expecting mothers. For example, it has yet to be explored how seizures or other neurological symptoms related to epilepsy may contribute to the risk of poor outcomes for both the mother and foetus.

When analysing postpartum haemorrhage, it has been demonstrated that preterm delivery, primary caesarean section, younger gestational age at delivery and anaemia were all linked to this motherly complication (Bazirete et al., 2022). Further studies have shown that postpartum haemorrhage has been linked with estimated blood loss greater than 500ml or an unnoticed decrease in haemoglobin levels by 2g/dl or more (Bazirete et al., 2022). Additionally, researchers have highlighted that mechanistic studies should be conducted to assess further information regarding any potential risk factors contributing to postpartum haemorrhage or even its severity (Bazirete et al., 2022). It has also been seen that stillbirths are associated with avoidable factors such as multidisciplinary regional audits (Sterpu et al., 2020), as well as low birth weights in babies born in Sulaimania City Iraq (Sardar Weli 2020). These results suggest a need for further research into how avoidable factors could be addressed in order to prevent stillbirths from occurring.

2.4.5 Other factors leading to maternal morbidity

Nyfløt et al. (2017) studied the risk factors associated with severe postpartum haemorrhage and conducted a case-control study in Norway settings. Pregnant women aged 18 to 50 with a singleton pregnancy were recruited. In the control group, the women who delivered after more than 37 weeks of gestation without postpartum haemorrhage within 24 hours of delivery were recruited. The cases were women who were diagnosed with a postpartum haemorrhage above 1,000 mL within 24 hours postpartum. Results showed that increased age, multiparity, cesarean delivery, instrumental delivery and induced labour increased the risk for postpartum haemorrhage among women in Norway. This study was well-designed and used appropriate sample sizes. Furthermore, it was based on hospital data providing reliable results. However, due

to the study being conducted only in Norway settings, its results may not necessarily be generalisable.

Esteves-Pereira et al. (2016) explored the association between Caesarian delivery and postpartum maternal mortality in Brazil by conducting a population-based case-control study that analysed mothers who died within 42 days following delivery due to causes related to pregnancy, labour or delivery as well as infants who died within 42 days after birth due to causes related to labour or delivery as cases. The study used controls who had successful deliveries. The results showed that mothers who underwent Caesarean deliveries are more likely to suffer postpartum maternal death than those who underwent vaginal deliveries. The methodology used was sensitive for measuring this association resulting in reliable findings but since the study was conducted only in Brazil the results may not be generalised.

Acosta et al. (2016) evaluated potential risk factors of severe sepsis among mothers during puerperium using a USA cohort study over 6 years from 2006 -2012. Some of the potential risk factors include preexisting medical conditions, comorbidities, multiple gestation and prolonged labour. The results showed that there is an increasing rate of maternal morbidity from severe sepsis. The sample size used was large enough and a reliable data source hence can be appropriate in clinical settings. Leonard et al. (2019) conducted a retrospective cohort study among deliveries over 10 years who had a cesarean delivery and investigated the relationship between cesarean delivery and the increased rate of severe maternal morbidity during puerperium in the USA setting. They observed that the C-section rate increased significantly over 10 years period due to increased medical indications hence older maternal age contributed dramatically to the rising rate of C-section rate. The findings showed that cesarean delivery was a strong predictor for severe maternal morbidity with increasing maternal age, further

exacerbating associated risks. The design and size of patients used enable an accurate understanding of the association between the C section. However, this article is limited by retrospective design which might lower its consistency because underlying conditions or events could have been lost over time or misunderstood during the collection process

Ben-Ayoun et al. (2023) conducted a population-based cohort study which analysed trends with potential predictors of severe peri-parturient maternal morbidity over the 10 years since 2010 in Israel set. They observed a significant increase in severe maternal morbidity of 9% with the lowest increase rate being seen in medical conditions and obstetric conditions accounting for the highest increases during the duration observed period. In addition, the length of stay was longer among cases than control growth with obstetrics conditions being associated with the highest or severity of medical morbidity compared to controls. The limitation of this article is the lack of data available on patient comorbidities which might have influenced study results.

It is evident from these studies that multiple factors could contribute towards severe maternal complications: age, parity, preexisting medical conditions, multiple pregnancies and length of labour are all important determinants for complications during pregnancy and childbirth. However, many studies have been limited by small sample sizes or confined geographical locations which limit their international applicability. It is important to analyze different patient attributes to develop a global understanding of these important issues and help reduce these preventable deaths across different countries and demographic backgrounds. However, this literature indicates that there are other critical factors which need to be considered when evaluating maternal morbidity due to complications.

Chapter 3: Methodology

3.1 Introduction

The methodology chapter of the research is important as it outlines the process that was used to determine the results and findings of the study (Kovach, 2015). This section outlines the research approach, data collection method, data analysis process and conclusions that were used to answer any research question or hypothesis. In the case of this systematic review, the methodology chapter is instrumental as it outlines the process of gathering relevant evidence for the topic.

3.2 Research design

The research design used for this study was a systematic review. Systematic reviews are commonly used to analyse research data related to a specific topic or condition in order to draw conclusions. This type of review allows the researcher to assess each individual evidence piece in relation to the topic or condition.

In this study, Medline, Cochrane and Cinahl databases were selected because they provide reliable and up-to-date health information. Additionally, both databases are well known for their coverage of health and medicine topics, provide access to full-text publications and feature a wide range of subject headings and keywords, which helps in ensuring more precise results.

3.3 Search strategy

The search term used in this study was “maternal morbidity” combined with “pre-eclampsia”, “traumatic brain injury” or “acquired brain injury”, and “epilepsy”. This search term was tailored specifically to this particular study’s aims, allowing the researcher to find relevant articles related to the topic. The inclusion criteria focused on articles related to the association of pre-eclampsia, traumatic/acquired brain injuries, and epilepsy in maternity and published within the past five

years. Exclusion criteria were set to exclude articles that lacked sufficient data for analysis or were not written in English. By setting these criteria, the researcher was able to reduce the number of irrelevant studies that did not fit the scope of the study.

The methodological quality of systematic reviews can also aid the research in denoting the strength and weaknesses of evidence from original research studies and thereby help to draw accurate conclusions (Pandey & Pandey, 2021). One advantage of systematic reviews is that they are able to identify and assess a wide variety of information in a short period of time. This is due to the fact that systematic reviews will often examine the information from numerous studies on a wide variety of topics (Zhang, Gong & Brown, 2023). By collating the data and cross-referencing the results of other studies, the systematic review can provide a comprehensive overview of the study topic.

The systematic review method used in this research has the advantage of being able to conduct a systematic investigation of a great deal of information in a brief time period, thereby providing a foundation for evidence-based conclusions about pre-eclampsia, traumatic/acquired brain injuries and epilepsy in maternity and maternal morbidity (Patel & Patel, 2019). This aspect was important for the current study considering the limited time for collecting and analysing data related to the topic of interest. The systematic review approach also provides a mechanism for subsequent confirmatory studies, as the results can be used to inform future studies or policymaking. Furthermore, the systematic approach may also be beneficial in assessing the costs and benefits of interventions involving the risk factors and morbidities in question.

3.4 Research Questions and Hypothesis

1. How does the occurrence of pre-eclampsia and/or traumatic/acquired brain injuries impact the rate of maternal morbidity?

2. How does the occurrence of epilepsy during the antenatal or postpartum period impact the rate of maternal morbidity?

3. What are the relative risk factors that contribute to these conditions during pregnancy?

4. Are there any protective factors that may reduce the severity or occurrence of one or all of these conditions?

3.4.1 Hypothesis

H1: Mothers who develop pre-eclampsia, traumatic/acquired brain injuries, or epilepsy are at a greater risk of developing post-partum complications and maternal morbidity.

H2: There are certain socio-demographic, medical and lifestyle risk factors which increase the risk of developing pre-eclampsia, traumatic/acquired brain injuries and/or epilepsy during the pregnancy period.

H3: Certain protective factors can help reduce the severity or occurrence of pre-eclampsia, traumatic/acquired brain injuries and/or epilepsy, thereby reducing the risk of maternal morbidity.

3.5 Validity and reliability

Validity and reliability are essential components of any research methodology, including the systematic review used here to assess possible risk factors contributing to maternal morbidity (Bull et al., 2019). Validity is a measure of a study's accuracy, or how well it measures what it

claims to measure while reliability is a measure of the consistency of results, which can help gauge the credibility of the study's findings (Quintão, Andrade & Almeida, 2020). These two components are essential for any meaningful research study, as valid and reliable results are necessary for sound conclusions to be determined.

Systematic reviews are particularly sensitive to validity, as they are less experimental in nature and rely more on other sources of evidence to conclude (Coleman, 2022). These sources may be of varying quality and reliability themselves, requiring that the review have mechanisms in place to assess the trustworthiness of included sources. Thus, assessments of validity must be conducted throughout the entire process of the review, from literature selection to analysis of the data. It is important to also consider sources of bias, or any source of error which affects the outcome of the research, as these may lead to invalid results.

The hallmark of using qualitative approaches such as systematic reviews arises from cost considerations (Rahman, 2020). This method is cheaper compared to quantitative methods which require the researcher to have a sufficient budget for collecting primary data. Thus, using this method in the current research contributed to cost-effectiveness in research. However, systematic reviews can also have their limitations. Due to the large quantity of data that needs to be assessed, it can be difficult to identify any biases or inherent weaknesses in the data. This can lead to significant errors in the conclusions drawn from the results (Voorhees & Howell Smith, 2020). Furthermore, the sheer volume of data may be difficult to handle efficiently and could lead to the selection of irrelevant sources or bias in data analysis, leading to invalid results. Therefore, considering these limitations in data collection is critical to attaining high-quality data.

3.6 Data collection

This study used a systematic review methodology in collecting data from the selected materials concerning the topic of study. Systematic reviews are an evidence-based methodology used in research to identify, appraise, and synthesize primary studies (Newman & Gough, 2020). This method was selected to study the topic of interest. Systematic reviews have been cited to be effective in providing an in-depth evaluation of a matter with a unified analysis by synthesizing data from different entities (Chen & Song, 2019).

3.7 Data analysis

This study used thematic analysis to analyse data obtained from the systematic review of pre-eclampsia, traumatic/acquired brain injuries and epilepsy in maternity. Thematic data analysis was used to identify and analyse the commonalities and differences between the data sets in the systematic review. This process of discovery begins with the initial coding of the data by the researcher and leads to the generation of themes and topics in the data (Neuendorf, 2018). This method involves the comparison of themes across the data sets, looking for patterns and relationships between the different evidence sources.

Data coding

Theme	Data Coding
1. Pre-eclampsia and morbidity	Maternal mortality rates, pre-eclampsia and eclampsia cases
	Maternal morbidity outcome measures
	Risk factors for pre-eclampsia and eclampsia
2. Traumatic brain injuries	Traumatic brain injury cases in pregnant women
	Acquired brain injuries in pregnant women
	Epilepsy in pregnant women

3. Cognitive deficits	Cognitive changes during pregnancy
	Neurological changes during pregnancy
4. Post-partum complications	Risk factors for post-partum complications
	Types of post-partum complications
5. Subarachnoid haemorrhage	Risk factors for subarachnoid haemorrhage in pregnancy
	Trauma in pregnancy and risk of subarachnoid haemorrhage

3.8 Conclusion

This chapter, therefore, presents key approaches adopted in collecting data from the identified materials. The adoption of a rigorous methodology is critical in ensuring that the research attains objectivity and thus, critical to the study's success. Invariably, this chapter contributes significantly to meeting the research objectives through a detailed analysis of the research approach.

Chapter 4. Results and Discussion

A total of one hundred and twenty-one (121) articles were obtained after the search process from the electronic databases.

4.0 Prisma Flow Chart

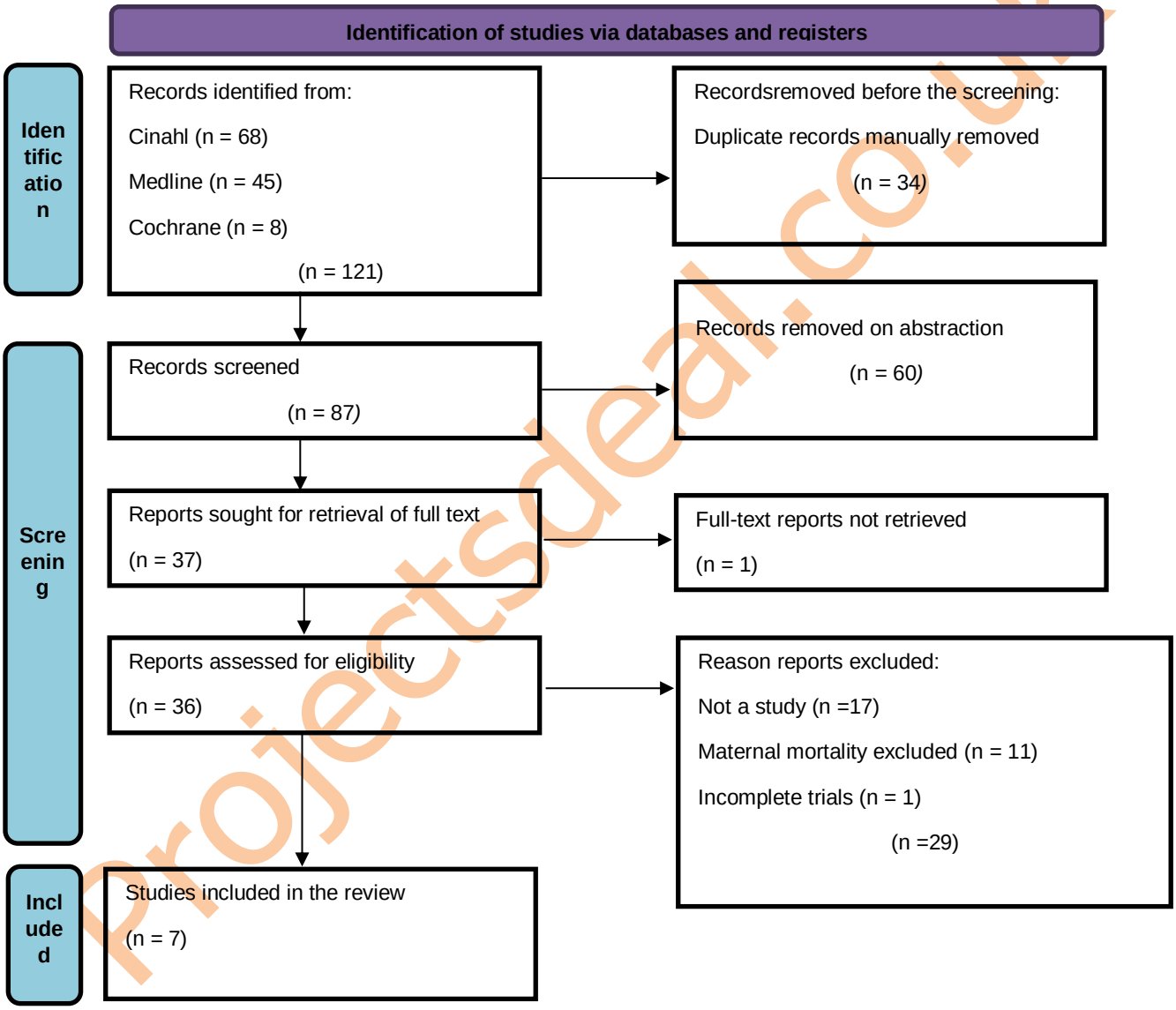

Figure 2.0 Prisma Flow Chart

4.1 Study characteristics

Authors	Methods	Sample	Results	Conclusion
Lolk et al. (2022)	Nationwide cohort study	Danish population	Perinatal adversities increase the risk of epilepsy after TBI	Perinatal adversities may be an important target for TBI prevention and epilepsy prophylaxis
Bokström-Rees et al. (2023)	The observational study, correlational	Women with pre-eclampsia and eclampsia	Cognitive assessment scores correlated with cerebral biomarkers	The correlation between cognitive assessment scores and cerebral biomarkers may aid in understanding the underlying pathophysiology of pre-eclampsia and eclampsia
Alan and Alan (2021)	Retrospective analysis	454 new-borns	Maternal hypertension, pre-eclampsia, and eclampsia associated	Maternal hypertension, pre-eclampsia, and eclampsia may have an impact on newborn hearing and warrant further investigation

			with hearing loss in new-borns	
Bahadur et al. (2022)	Retrospective analysis	Women with pre-eclampsia/eclampsia	Factors associated with PRES identified	Early identification of PRES risk factors can aid in prompt management and improved outcomes
Korhonen et al. (2023)	Population-based study	Finnish women with subarachnoid haemorrhage during pregnancy	Risk factors identified for SAH during pregnancy and puerperium	SAH during pregnancy and puerperium is associated with high morbidity and mortality rates, highlighting the need for improved management and prevention strategies
Tran et al. (2019)	Case-control study	Singleton pregnancies in Reunion Island	Risk factors identified for recurrent preeclampsia in multiparae	Early identification of risk factors for recurrent preeclampsia in multiparae can aid in prevention and improved outcomes
Vaajala et al. (2022)	Population-based cohort study	Fertile-aged women in Finland with major trauma	The birth rate is significantly lower in	Women with major trauma should be provided with appropriate counselling and support regarding fertility

			women with major trauma compared to controls	and family planning

Table 1.0 Study Characteristics

The seven studies chosen for this systematic review used a combination of quantitative, qualitative, and mixed-methods approaches to investigate the metrics under study. Lolk et al. (2022) used a descriptive epidemiological design to analyse a nationwide cohort study in Denmark, documenting maternal exposures and outcomes of epilepsy in relationship to prenatal adversities and pre-eclampsia. The researchers measured data on prenatal exposures (i.e., pre-eclampsia, traumatic brain injury, amongst others), and measured outcomes for those exposed to pre-eclampsia and traumatic brain injuries (i.e. epilepsy). The study also accounted for other potential confounding variables. Bokström-Rees et al. (2023) used a descriptive epidemiological design to investigate the relationship between cognitive assessment scores and circulating cerebral biomarkers in pre-eclamptic and eclamptic women. They administered cognitive tests and gathered blood samples to measure cerebral biomarkers.

Alan and Alan (2021) also used a descriptive epidemiological design to assess the relationship between maternal hypertension, pre-eclampsia, eclampsia and newborn hearing. This study measured the hearing of newborns in relation to pre-eclampsia, eclampsia and maternal hypertension. The fourth article by Bahadur et al. (2022) used a retrospective analysis to investigate the predictors of posterior reversible encephalopathy syndrome (PRES) in women with pre-eclampsia and eclampsia. It utilized a case-control format to assess clinical characteristics and laboratory results. The fifth article by Korhonen et al. (2023) used a

population-based study to investigate the association between subarachnoid haemorrhage during pregnancy and puerperium. They recorded data on demographic, neurological, and medical characteristics, and categorized haemorrhage into early, late and recurrent. The sixth article by Tran et al. (2019) used a case-control study to investigate the potential risk factors responsible for recurrent pre-eclampsia in non-singleton pregnancies. The researchers analysed data from Reunion Island on demographic factors, lifestyle characteristics and anthropometric measurements.

Vaajala et al. (2022) used a nationwide cohort study to investigate the birth rate of pregnant women after major trauma. This study measured both pre- and post-traumatic factors and also accounted for lifestyle, comorbidity, and social/psychological characteristics. Across the seven studies, a variety of study designs have been utilized to investigate the topic of focus. The most common designs included descriptive epidemiological, case-control, and retrospective analyses. Of the seven studies included in the review, two were population-based cohort studies, two retrospective studies, one national-wide cohort study, a case-control study and an observational study. The diverse range of designs allowed for an in-depth analysis of various factors influencing maternal morbidity. This systematic review provides an important contribution to the literature and helps to fill the gaps in knowledge concerning these risk factors.

4.2 Discussion

Based on the articles analysed in this study, several common themes emerged which are subject to critical evaluation. These themes are discussed in the following sections.

4.2.1 Pre-eclampsia, eclampsia and maternal morbidity

Pre-eclampsia, eclampsia, and other hypertensive disorders are potential risk factors for maternal morbidity. Most studies suggest that maternal Hypertensive disorders during pregnancy are associated with a higher risk of neonatal morbidity and mortality in the event of eclampsia or pre-eclampsia (Lolk et al., 2022; Bokström-Rees et al., 2023). This increased risk is, in part, due to the rapid onset and nature of the condition, which can lead to sudden organ dysfunction and serious complications for mother and baby if left untreated. In addition to the risks associated with Hypertensive disorders, some studies have suggested that pre-eclampsia and eclampsia may be risk factors for maternal epileptic seizures (Bokström-Rees et al., 2023; Alan & Alan, 2021). This is of particular concern as the impact of such seizures may be more severe in pregnant women than in non-pregnant women. These articles suggest that pre-eclampsia, eclampsia and other hypertensive disorders of pregnancy are associated with a significant increase in the risk of developing epilepsy in the mother. This increased risk was found to be greater in mothers who suffered from a pre-existing condition prior to the pregnancy, such as diabetes, bariatric, perinatal adversity, or seizures. Furthermore, the articles discussed findings that pre-eclampsia, eclampsia and other hypertensive disorders of pregnancy could be associated with an increased risk of other neuropsychiatric and cognitive deficits in the mother, such as cognitive delays and neurodevelopmental impairments.

Traumatic or acquired brain injuries have also been identified as a potential risk factor for both maternal and neonatal morbidity (Korhonen et al., 2023). Research has suggested that antenatal brain injury is associated with a higher risk of pre-term birth, fetal growth restriction, placental abnormalities and low Apgar score (Korhonen et al., 2023; Tran et al., 2019). Such injuries can also lead to neurological impairments for the child if left untreated, with some studies

demonstrating a link between traumatic brain injury during pregnancy and an increased risk of childhood epilepsy (Tochio et al., 2019).

Also, the findings suggest that pre-eclampsia and eclampsia may both be associated with an increased risk of posterior reversible encephalopathy syndrome (PRES) in women (Bahadur et al., 2022). PRES is a neurological disorder characterised by increased intracranial pressure, seizures, and stroke-like symptoms which are reversible with prompt treatment (Fischer & Schmutzhard, 2017). It can result in serious complications if left untreated and is a particularly concerning health issue for pregnant women who may already be at increased risk of hypertension and other associated disorders. Therefore, it is imperative to consider this attribute during maternity to improve the quality of life for women.

4.2.2 Traumatic and acquired brain injuries and Epilepsy in Women

The studies discussed in this systematic review highlight the correlation between traumatic and acquired brain injuries, pre-eclampsia and epilepsy in women. Studies included in this systematic review analyse the prevalence of neurological conditions such as recurrent pre-eclampsia, subarachnoid haemorrhage and posterior reversible encephalopathy syndrome attributed to pre-eclampsia/eclampsia. Furthermore, the risk of epilepsy associated with traumatic brain injuries in mothers is also discussed.

A systematic review by Lolk et al. (2022), examines the association between traumatic brain injury and the risk of epilepsy. The study found that there was an increased risk of epilepsy in mothers who experienced a traumatic brain injury at a later age. The study further showed that both the duration and the severity of the traumatic brain injury increased the risk of developing epilepsy.

Similarly, Alan and Alan (2021) examine the association between maternal hypertension pre-eclampsia, eclampsia, and hearing in newborns. The study found that the presence of maternal hypertension or pre-eclampsia/eclampsia increased the risk of hearing loss in newborns. The study further showed that longer gestational exposure to maternal hypertension was a risk factor for increased hearing impairment. The study by Bahadur et al. (2022) examines the predictors of posterior reversible encephalopathy syndrome (PRES) in pregnant women. The study found that PRES was significantly predicted by higher systolic blood pressure, lower platelet counts and higher levels of glucose.

Korhonen et al. (2023) focus on subarachnoid haemorrhage that occurs during pregnancy and the puerperium. The study found that subarachnoid haemorrhage is a rare event, but could be associated with an increased risk of epilepsy. Finally, Tran et al. (2019) and Vaajala et al. (2022) investigate the correlation between recurrent pre-eclampsia, traumatic brain injury and the risk of childbirth in mothers. The study found that recurrent pre-eclampsia increases the risk of childbirth in mothers. Likewise, traumatic brain injury was found to be associated with the risk of childbirth, albeit to a lesser extent.

Thus, these studies demonstrate that both pre-eclampsia and traumatic brain injury can be risk factors for epilepsy in women. Furthermore, pre-eclampsia has been linked to cognitive impairment and hearing impairments in newborns, as well as an increased risk of childbirth in mothers (Sterpu et al., 2020). Additionally, traumatic brain injury has been found to have a strong association with the risk of developing epilepsy. Hence, healthcare providers should be aware of the potential risks associated with pre-eclampsia and traumatic brain injury in pregnant mothers, as they could be associated with an increased risk of neurological complications.

4.2.3 Cognitive Deficits and neurological changes in Pregnancy

Cognitive deficits and neurobiological changes are common in women with preeclampsia, a hypertensive disorder that occurs during the second half of pregnancy (Newman & Gough, 2020). Preeclampsia is associated with permanent adverse outcomes such as preterm birth and an increased risk of developing neurological disorders in the mother, namely cognitive decline, traumatic brain injury and epilepsy. Thus, it is important to understand the foundations of these conditions in order to optimise maternal care.

The importance of cognitive deficits in women with preeclampsia has been discussed in a recent study by Bokström-Rees et al. (2023). This study evaluated the correlation between cognitive assessment scores and circulating cerebral biomarkers in women with preeclampsia and eclampsia. The authors found that women with higher scores in tests of verbal memory and executive function were more likely to have higher levels of biomarkers associated with neural injury (e.g., glial fibrillary acidic protein, total tau and S100 proteins). This suggests that preeclampsia may lead to subtle changes in cognitive functioning that are detectable with neurobiological markers.

Similarly, a study by Alan et al. (2021) found that prenatal hypertension and preeclampsia were negatively correlated with a range of neonatal hearing outcomes (such as hearing thresholds, otoacoustic emissions, and auditory brainstem response). These results illustrate how even mild cognitive impairments associated with preeclampsia can have serious consequences for fetal development. Moreover, Lolk et al. (2022) found that preeclampsia was associated with an increased risk of developing epilepsy after traumatic brain injury. This suggests that preeclampsia may predispose an individual to increased vulnerability for subsequent neurological injury.

Despite some of the physiological differences between pre-eclampsia and other conditions such as traumatic/acquired brain injuries, it has been suggested that similar peripheral and central mechanisms may play a role in both cases. For example, Korhonen et al. (2023) proposed that changes in sympathetic nervous system function and changes in neurotransmission may be shared between pre-eclampsia and subarachnoid haemorrhage. Similarly, Tran et al. (2019) reported that recurrent preeclampsia was associated with an increased risk of developing posterior reversible encephalopathy syndrome (PRES). This indicates that there may be a shared pathophysiology allowing for increased maternal morbidity across conditions.

Therefore, it is apparent that cognitive deficits and neurobiological changes in women with preeclampsia can have serious consequences. The evidence discussed in this review suggests that preeclampsia may predispose an individual to a higher risk of developing other conditions such as trauma/acquired brain injury and epilepsy in the future. Further research, such as prospective studies and larger sample sizes, may help to elucidate the relationship between preeclampsia and maternal morbidity and inform further interventions to protect women from cognitive decline and neurological injury.

4.2.4 Risk factors for post-partum complications

Postpartum complications can affect both mother and child. Maternal postpartum complications include infections, major bleeding, thrombosis, cardiopulmonary complications, pain, mental health issues, endocrine problems, and other chronic conditions (Menon & Irving, 2022). Pregnancy itself increases the risk of morbidity due to the physical and emotional stress of delivery and subsequent recovery. Previous studies have identified pre-existing risk factors for maternal postpartum problems such as pre-eclampsia, traumatic or acquired brain injury, and epilepsy. Studies have found that women with pre-eclampsia had an increased risk of postpartum

complications including infections and cardiopulmonary events (Graham et al., 2021). Women with pre-eclampsia are also more likely to experience mental health issues such as depression and anxiety.

The research has also revealed a link between traumatic or acquired brain injury and postpartum complications. A Danish nationwide cohort study by Lolk et al. (2022) showed a significant increase in the risk of developing epilepsy after a traumatic brain injury. Furthermore, this study found an increased incidence of problems including bleeding, haematomas, infections, and cardiopulmonary complications in women with traumatic brain injuries.

Epilepsy is another risk factor for postpartum problems. A recent retrospective analysis of 454 newborns by Alan and Alan (2021) showed that maternal hypertension, pre-eclampsia, and eclampsia are associated with an increased risk of developing epilepsy in the mother. Similar results were found in a retrospective analysis of women with pre-eclampsia/eclampsia by Bahadur et al. (2022), which showed a strong correlation between cognitive assessment scores and circulating cerebral biomarkers. In addition, a population-based study by Korhonen et al. (2023) found an increased risk of subarachnoid haemorrhage in women with epilepsy during pregnancy and postpartum.

Recurrent pre-eclampsia is also associated with an increased risk for issues related to childbirth. Tran et al. (2019) conducted a case-control study and found that the risk of maternal morbidity and mortality was significantly increased among multiparous women who had recurrent pre-eclampsia or a first episode of pre-eclampsia. Similarly, a nationwide population-based cohort study by Vaajala et al. (2022) revealed that women with major trauma have a higher risk of morbidity and mortality during labour, delivery, and in the postpartum period.

4.2.5 Pregnancy and Risk of Subarachnoid Hemorrhage and major trauma

Pregnancy is associated with numerous physical and physiological changes, presenting expectant mothers with a wide range of risks and complications that can arise during or after delivery (Darlan et al., 2021). Major trauma and subarachnoid haemorrhage (SAH) are among these risks, representing serious medical issues with potentially devastating consequences for pregnant women and their newborns. The purpose of this discussion is to evaluate the results of the current literature to assess the relationship between pregnancy and the risk of SAH and major trauma.

Studies conducted by Korhonen et al. (2023) and Vaajala et al. (2022) investigated the possible relationship between pregnancy and major trauma or SAH. Korhonen et al. (2023) conducted a population-based study to examine SAH during pregnancy, including 22 cases of the disease found among 2,757,705 pregnancies between 1997-2016. Associations were found between SAH and previous SAH and hypertension, confirming the role of these factors in the incidence of SAH during pregnancy. Vaajala et al. (2022) similarly analysed the risk of major trauma among pregnant women in Finland. This study found a significantly increased risk of trauma in reproductive-age women when compared to the general population. Notably, however, the cumulative risk of major trauma among pregnant women remained low, indicating that caution and regular medical supervision are necessary to identify risk factors and intervene when necessary.

Pre-eclampsia and eclampsia are other risk factors explored in relation to the risk of SAH and major trauma associated with pregnancy. Bokström-Rees et al. (2023) investigated links between pre-eclampsia and cognitive impairment, while Alan & Alan (2021) used a retrospective analysis of 454 newborns to discover a correlation between maternal hypertension and newborn hearing

impairment. These studies demonstrated positive associations between preeclampsia and related conditions and a higher risk of cognitive impairment and hearing impairment respectively. Additionally, Tran et al. (2019) conducted a case-control study to assess the risk of recurrent pre-eclampsia in multiparous women. The results suggested that there was an increased risk of recurrent pre-eclampsia in multiple pregnancies, highlighting the necessity of closely monitoring the mother in such cases. Further, Lolk et al. (2022) analysed the risk of epilepsy after traumatic brain injury in pregnant and non-pregnant women. The study concluded that pre-eclampsia, traumatic brain injury, and epilepsy are all interlinked in maternity, accepting the presence of these conditions during pregnancy may increase the risk of severe medical issues and the need for specialist medical attention.

Chapter 5. Conclusion

The current literature suggests an association between pregnancy and increased risk of major trauma, subarachnoid haemorrhage, as well as complications such as pre-eclampsia, epilepsy and cognitive impairment. These studies highlight the importance of closely monitoring pregnant mothers and providing them with appropriate medical treatment and assistance to minimize the risks associated with preeclampsia and major trauma (Black et al., 2015). Multiparous women, in particular, require additional medical attention and monitoring as the presence of pre-eclampsia during multiple pregnancies appears to further increase the risk of medical-related adverse effects. Meanwhile, supporting the mother to manage pre-eclampsia and related conditions through lifestyle modifications and good nutrition may help reduce the risks associated with maternal morbidity. Thus, it is essential to recognize the risks of traumatic brain injuries, SAH and pre-eclampsia during pregnancy, with attention to early detection and appropriate medical assistance.

Based on the systematic review, the results gathered point towards a relationship between pre-eclampsia, traumatic/acquired brain injuries and epilepsy. For example, studies found that women with both pre-eclampsia and traumatic brain injuries had an increased risk of suffering from epilepsy than those without comorbidities (Bokström-Rees et al., 2023; Lolk et al., 2022). Additionally, the findings indicated that women with preeclampsia/eclampsia were more likely to suffer from posterior reversible encephalopathy syndrome (PRES) and major trauma in fertility-aged women increased the chance of birth rate compared to women without trauma. Based on this review, it can be concluded that there is a potential relationship between pre-eclampsia, traumatic/acquired brain injuries and epilepsy in maternity.

Another important finding from this study is the association between comorbidities and maternal morbidity during maternity Multiple studies revealed that women with pre-eclampsia are more likely to suffer from neurological deficits, such as cognitive deficits and hearing impairments, as well as an increased risk of developing epilepsy. Other factors, such as traumatic or acquired brain injuries, have also been found to be a risk factors in the development of epilepsy in the pregnant population (Voorhees & Howell Smith, 2020). Furthermore, an association has also been demonstrated between pre-eclampsia, brain injuries and posterior reversible encephalopathy syndrome (PRES) in women. It is important to note that due to the limited number of studies included in this systematic review, the findings should be interpreted with caution. A majority of the studies included in this review had small sample sizes, which could impact the accuracy and generalizability of the results. Furthermore, due to the heterogenic nature of the studies included in this systematic review, the comparability of the results was also limited.

It appears from this systematic review that pre-eclampsia is a risk factor for increased maternal morbidity. This review found that there is a strong association between pre-eclampsia and both maternal mortality and morbidity. Most studies analysed concluded that the presence of pre-eclampsia in the mother has a significant impact on the outcome of her pregnancy (Sterpu et al., 2020; Shoopala& Hall, 2019; Miller et al., 2022). This can range from an increased risk of maternal death to an increased risk of long-term health problems and adverse development outcomes. Given the prevalence of pre-eclampsia, it is important to screen for this condition in pregnancy and to provide support and treatment.

Also, this systematic review also revealed evidence to suggest that epilepsy presents an additional risk factor for increased maternal morbidity. The studies reviewed provided evidence to suggest that epilepsy is associated with a higher prevalence of certain medical complications,

such as preterm delivery, low birth weight, and gestational diabetes. In addition, the review found that there is an increased risk of adverse neonatal outcomes in the presence of epilepsy, such as neurological morbidities, preterm delivery, and low birth weight (Bahadur et al., 2022). Maternal morbidity caused by these conditions is an important public health concern, and so understanding the causes of such conditions is paramount to their prevention and effective management. Moreover, due to the increasingly greater numbers of women with acquired brain injuries delivering in maternity, the need to be able to identify the risk factors associated is becoming increasingly important.

The results of this systematic review show that there may be a significant risk associated with pre-eclampsia, which affects between 5-10% of pregnant women. This condition can cause a number of complications, including premature delivery, low birth weight, and even death. In addition, pre-eclampsia has been linked to increased risks of developing chronic diseases in the mother, such as cardiovascular and renal disease, which can have far-reaching consequences in terms of quality of life and life expectancy.

Based on the evidence presented in this systematic review, the developed hypothesis is supported. Further research is needed to investigate these topics in more detail and to better understand the potential risk factors that may be contributing to maternal morbidity. Finally, the results of this review indicate that there may be an association between epilepsy, preterm delivery and an increased risk of maternal morbidity, including postpartum haemorrhage, operative delivery, and perinatal mortality. This underscores the importance of screening and early management of this condition in order to reduce the risks associated with it. Therefore, this study adopts the hypothesis that pre-eclampsia and other comorbidities impact on maternal morbidity. Also, the occurrence of epilepsy impacts on the rate of maternal morbidity.

Chapter 6. Recommendations

The hypothesis that socio-demographic, medical and lifestyle risk factors increase the risk of pre-eclampsia, traumatic/acquired brain injuries and/or epilepsy during pregnancy, and that protective factors can help reduce the severity or occurrence of these conditions, can be confirmed by the evidence presented in this systematic review. In particular, socio-economic status, such as poverty, was identified as a risk factor for poorer maternal health outcomes and an increased risk of pre-eclampsia, traumatic/acquired brain injuries and/or epilepsy. Low-income households are more likely to experience multiple stressors and lack access to adequate healthcare, which can lead to poor health outcomes during pregnancy. Additionally, these households may not be able to afford the recommended lifestyle changes associated with a healthy pregnancy, such as healthy eating, physical activity and stress management.

To address the problem of poverty and its associated risk of pre-eclampsia, traumatic/acquired brain injuries and/or epilepsy, there may need to be provision of financial support or signposting to support services. This could include access to food banks, social benefits and adequate healthcare. Furthermore, providing access to education and health promotion initiatives can help women to make informed decisions about their lifestyle and health during pregnancy. This is especially important for women from low-income households, who may not have the same access to healthcare and lifestyle advice as those from more affluent backgrounds. Ultimately, if these issues are addressed, it is likely that the risk of pre-eclampsia, traumatic/acquired brain injuries and/or epilepsy can be reduced, and the incidence of maternal morbidity decreased.

Healthcare providers should be educated and trained on how to effectively manage and prevent pre-eclampsia. This includes educating and training providers on how to recognize the signs and symptoms of pre-eclampsia, and how to provide appropriate treatments and interventions to

reduce the risk of developing neurological disabilities (Mol et al., 2016). Providers should also be informed about the potential links between pre-eclampsia and other neurological conditions and should be made aware of warning signs and triggers that may result from pre-eclampsia that can lead to other neurological disabilities.

Also, efforts should be made to encourage pregnant women, who are either at high risk or have already been diagnosed with pre-eclampsia, to seek early and regular prenatal care. Regular prenatal care can help to identify and monitor pre-eclampsia and can provide appropriate interventions to reduce the risk of complications, such as neurological disabilities, associated with the condition.

Finally, given the limited number of scholarly articles that were reviewed for this study, it is recommended to conduct further research on this topic. This should include additional studies that focus on the potential for preventative and treatment interventions during maternity to prevent maternal morbidity. In addition, more high-quality meta-analyses and systematic reviews would provide a more comprehensive understanding of the study topic.

The results of this systematic review suggest a link between pre-eclampsia, traumatic/acquired brain injuries and epilepsy in maternity and an increased risk of post-partum complications and maternal morbidity. Pre-eclampsia has been shown to be associated with an increased risk of stroke, eclampsia, and cesarean section, as well as an increased risk of placental abruption and preterm birth. Traumatic or acquired brain injuries have been linked to an increased risk of preterm birth, preterm labor, fetal distress, and postpartum hemorrhage. Epilepsy has been linked to an increased risk of preterm labor and preterm birth, as well as an increased risk of stillbirth, low birth weight and neonatal seizures.

In support of the second hypothesis, this systematic review found evidence of certain socio-demographic, medical and lifestyle risk factors that increase the risk of developing pre-eclampsia, traumatic/acquired brain injuries and/or epilepsy during the pregnancy period. These risk factors include advanced maternal age, pre-existing hypertension and diabetes, and lifestyle factors such as smoking and alcohol use.

In support of the third hypothesis, certain protective factors can help reduce the severity or occurrence of pre-eclampsia, traumatic/acquired brain injuries and/or epilepsy, thereby reducing the risk of maternal morbidity. These protective factors include regular antenatal care, lifestyle modifications such as quitting smoking and limiting alcohol intake, and good nutrition and supplementation with essential vitamins and minerals, such as vitamin E and magnesium.

Pre-eclampsia, traumatic/acquired brain injuries, and epilepsy have all been linked to higher rates of maternal morbidity. Therefore, it is necessary for healthcare practitioners to proactively assess and monitor for these risks during antenatal care and provide appropriate prevention, risk reduction, and treatment strategies. By doing this, healthcare practitioners can reduce the overall morbidity associated with these conditions and optimize the health of the mother and baby.

References

Acosta, C. D., Harrison, D. A., Rowan, K., Lucas, D. N., Kurinczuk, J. J., & Knight, M. (2016). Maternal morbidity and mortality from severe sepsis: a national cohort study. BMJ open, 6(8), e012323.http://dx.doi.org/10.1136/bmjopen-2016-012323.

Adlam, J. A. (2021). Early onset pre-eclampsia with severe features necessitating fetal delivery: Outcome of pregnancies with birthweight 1000-1800g at Tygerberg Hospital 2017.ttp://dx.doi.org/10.1136/bmjopen-2016-4325.

Al Bizri, A. et al. (2021) "Timing of term elective cesarean section and adverse neonatal outcomes: A multi-centre retrospective cohort study," PloS one, 16(4), p. e0249557.https://doi.org/10.1371/journal.pone.0249557.

Al Fauzi, A., Apriawan, T., Ranuh, I. A. R., Christi, A. Y., Bajamal, A. H., Turchan, A., ... & Kasper, E. M. (2023). Traumatic brain injury in pregnancy: A systematic review of epidemiology, management, and outcome. Journal of clinical neuroscience, 107, 106-117.10.1016/j.jocn.2022.12.007

Alan, C., & Alan, M. A. (2021). Maternal hypertension, pre-eclampsia, eclampsia and newborn hearing: A retrospective analysis of 454 newborns. International Journal of Pediatric Otorhinolaryngology, 146, 110748.https://doi.org/10.1016/j.ijporl.2021.110748.

Jazdarehee, A., Huget-Penner, S. and Pawlowska, M. (2022) 'Pseudo-pheochromocytoma due to obstructive sleep apnea: a case report', Endocrinology, diabetes & metabolism case reports, 2022(1), pp. 1–4. Available at: https://doi.org/10.1530/EDM-21-0100.

Bahadur, A., Mundhra, R., Singh, R., Mishra, J., Suresh, G., Jaiswal, S., Sinha, D. and Singh, M. (2022) 'Predictors of Posterior Reversible Encephalopathy Syndrome (PRES) in Women With Pre-eclampsia/Eclampsia: A Retrospective Analysis', Curēus (Palo Alto, CA), 14(11), pp. e31459–e31459. Available at: https://doi.org/10.7759/cureus.31459.

Bahri Khomami, M., Joham, A.E., Boyle, J.A., Piltonen, T., Silagy, M., Arora, C., Misso, M.L., Teede, H.J. and Moran, L.J. (2019) 'Increased maternal pregnancy complications in polycystic ovary syndrome appear to be independent of obesity—A systematic review, meta-analysis, and meta-regression', Obesity reviews, 20(5), pp. 659–674. Available at: https://doi.org/10.1111/obr.12829.

Baschat, A.A., Dewberry, D., Seravalli, V., Miller, J.L., Block-Abraham, D. and Blitzer, M.G. (2018) 'Maternal blood-pressure trends throughout pregnancy and development of pre-eclampsia in women receiving first-trimester aspirin prophylaxis', Ultrasound in obstetrics & gynaecology, 52(6), pp. 728–733. Available at: https://doi.org/10.1002/uog.18992.

Bazirete, O., Nzayirambaho, M., Umubyeyi, A., Karangwa, I. and Evans, M. (2022) 'Risk factors for postpartum haemorrhage in the Northern Province of Rwanda: A case control study', PloS one, 17(2), pp. e0263731–e0263731. Available at: https://doi.org/10.1371/journal.pone.0263731.

Ben-Ayoun, D., Walfisch, A., Wainstock, T., Sheiner, E. and Imterat, M. (2023) 'Trend and risk Factors for Severe Peripartum Maternal morbidity - a population-based Cohort Study', Maternal and child health journal, 27(4), pp. 719–727. Available at: https://doi.org/10.1007/s10995-022-03568-2.

Bergman, L., Zetterberg, H., Kaihola, H., Hagberg, H., Blennow, K. and Åkerud, H. (2018) 'Blood-based cerebral biomarkers in preeclampsia: Plasma concentrations of NfL, tau, S100B and NSE during pregnancy in women who later develop preeclampsia - A nested case control study', PloS one, 13(5), pp. e0196025–e0196025. Available at: https://doi.org/10.1371/journal.pone.0196025.

Bijl, R.C., Bangert, S.E., Shree, R., Brewer, A.N., Abrenica-Keffer, N., Tsigas, E.Z., Koster, M.P.H. and Seely, E.W. (2022) 'Patient journey during and after a pre-eclampsia-complicated pregnancy: a cross-sectional patient registry study', BMJ open, 12(3), pp. e057795–e057795. Available at: https://doi.org/10.1136/bmjopen-2021-057795.

Black, A.M., Armstrong, E.A., Scott, O., Juurlink, B.J.H. and Yager, J.Y. (2015) 'Broccoli sprout supplementation during pregnancy prevents brain injury in the newborn rat following placental insufficiency', Behavioural brain research, 291, pp. 289–298. Available at: https://doi.org/10.1016/j.bbr.2015.05.033.

Bokström-Rees, E., Zetterberg, H., Blennow, K., Hastie, R., Schell, S., Cluver, C. and Bergman, L. (2023) 'Correlation between cognitive assessment scores and circulating cerebral biomarkers in women with pre-eclampsia and eclampsia', Pregnancy hypertension, 31, pp. 38–45. Available at: https://doi.org/10.1016/j.preghy.2022.12.001.

Bull, C., Byrnes, J., Hettiarachchi, R. and Downes, M. (2019) 'A systematic review of the validity and reliability of patient-reported experience measures', Health services research, 54(5), pp. 1023–1035. Available at: https://doi.org/10.1111/1475-6773.13187.

Cerdeira, A., Agrawal, S., Staff, A., Redman, C. and Vatish, M. (2018) 'Angiogenic factors: potential to change clinical practice in pre-eclampsia?', BJOG : an international journal of

obstetrics and gynaecology, 125(11), pp. 1389–1395. Available at: https://doi.org/10.1111/1471-0528.15042.

Chen, C. and Song, M. (2019) 'Visualizing a field of research: A methodology of systematic scientometric reviews', PloS one, 14(10), pp. e0223994–e0223994. Available at: https://doi.org/10.1371/journal.pone.0223994.

Chu, J., Johnston, T.A. and Geoghegan, J. (2020) 'Maternal Collapse in Pregnancy and the Puerperium: Green-top Guideline No. 56', BJOG : an international journal of obstetrics and gynaecology, 127(5), pp. e14–e52. Available at: https://doi.org/10.1111/1471-0528.15995.

Coleman, P. (2021) 'Validity and Reliability within Qualitative Research in the Caring Sciences', International journal of caring sciences, 14(3), pp. 2041–2045.ISSN 1792-037X

Danielsson, K.C., Borthen, I., Gilhus, N.E. and Morken, N.H. (2018) 'The effect of parity on risk of complications in pregnant women with epilepsy: a population-based cohort study', Acta obstetricia et gynecologica Scandinavica, 97(8), pp. 1006–1014. Available at: https://doi.org/10.1111/aogs.13360.

Darlan, D., Prasetya, G., Ismail, A., Pradana, A., Fauza, J., Dariansyah, A., Wardana, G., Apriawan, T. and Bajamal, A. (2021) 'Algorithm of traumatic brain injury in pregnancy (Perspective on neurosurgery)', Asian journal of neurosurgery, 16(2), pp. 249–257. Available at: https://doi.org/10.4103/ajns.AJNS_243_20.

Dimitriadis, E., Rolnik, D. L., Zhou, W., Estrada-Gutierrez, G., Koga, K., Francisco, R. P., ... & Menkhorst, E. (2023). Pre-eclampsia. Nature Reviews Disease Primers, 9(1), 8.https://doi.org/10.1038/s41572-023-00417-6.

Duffy, J., Thompson, T., Hinton, L., Salinas, M., McManus, R., Ziebland, S., Barnard, A.M., Crawford, C., Dennis, T., Johnson, M., Khan, R., Newhouse, L., Sandhu, G., Shalofsky, T., Waite, L., Wilson, M. and Khan, K.S. (2019) 'What outcomes should researchers select, collect and report in pre-eclampsia research? A qualitative study exploring the views of women with lived experience of pre-eclampsia', BJOG : an international journal of obstetrics and gynaecology, 126(5), pp. 637–646. Available at: https://doi.org/10.1111/1471-0528.15616.

Esteves-Pereira, A.P., Deneux-Tharaux, C., Nakamura-Pereira, M., Saucedo, M., Bouvier-Colle, M.-H. and Leal, M. do C. (2016) 'Caesarean Delivery and Postpartum Maternal Mortality: A Population-Based Case Control Study in Brazil', PloS one, 11(4), pp. e0153396–e0153396. Available at: https://doi.org/10.1371/journal.pone.0153396.

Farnaaz, D. S., student, P., & manjunatheshwara, S. D. (2022). The maternal and fetal outcome of eclampsia in a tertiary care hospital.https://doi.org/10.1038/245321-023-00417-6.

Fischer, M. and Schmutzhard, E. (2017) 'Posterior reversible encephalopathy syndrome', Journal of neurology, 264(8), pp. 1608–1616. Available at: https://doi.org/10.1007/s00415-016-8377-8.

Gambhir, S., Grigorian, A., Schubl, S., Barrios, C., Bernal, N., Joe, V., Gabriel, V. and Nahmias, J. (2019) 'Analysis of non-obstetric vaginal and vulvar trauma: risk factors for operative intervention', Updates in surgery, 71(4), pp. 735–740. Available at: https://doi.org/10.1007/s13304-019-00679-4.

Giovanna Marchini., Martín Muñoz, D. and Vladic Stjernholm, Y. (2020) 'A parietal bone fracture with subgaleal and subdural hemorrhage in association with vacuum extraction

delivery', Clinical case reports, 8(11), pp. 2103–2106. Available at: https://doi.org/10.1002/ccr3.2119.

Graham, L.M., Sahay, K.M., Rizo, C.F., Messing, J.T. and Macy, R.J. (2021) 'The Validity and Reliability of Available Intimate Partner Homicide and Reassault Risk Assessment Tools: A Systematic Review', Trauma, Violence, & Abuse, 22(1), pp. 18–40. Available at: https://doi.org/10.1177/1524838018821952.

Han, X., Huang, Q., Liu, L., Sha, X., Hu, B. and Liu, H. (2018) 'Changes in the Expression of AQP4 and AQP9 in the Hippocampus Following Eclampsia-Like Seizure', International journal of molecular sciences, 19(1), p. 300–. Available at: https://doi.org/10.3390/ijms19010300.

Hayes-Ryan, D., Hemming, K., Breathnach, F., Cotter, A., Devane, D., Hunter, A., McAuliffe, F.M., Morrison, J.J., Murphy, D.J., Khashan, A., McElroy, B., Murphy, A., Dempsey, E., O'Donoghue, K. and Kenny, L.C. (2019) 'PARROT Ireland: Placental growth factor in Assessment of women with suspected pre-eclampsia to reduce maternal morbidity: a Stepped Wedge Cluster Randomised Control Trial Research Study Protocol', BMJ open, 9(2), pp. e023562–e023562. Available at: https://doi.org/10.1136/bmjopen-2018-023562.

Hirshberg, A. and Srinivas, S.K. (2017) 'Epidemiology of maternal morbidity and mortality', Seminars in perinatology, 41(6), pp. 332–337. Available at: https://doi.org/10.1053/j.semperi.2017.07.007.

Högberg, U., Andersson, J., Squier, W., Högberg, G., Fellman, V., Thiblin, I. and Wester, K. (2018) 'Epidemiology of subdural haemorrhage during infancy: A population-based register study', PloS one, 13(10), pp. e0206340–e0206340. Available at: https://doi.org/10.1371/journal.pone.0206340.

Irving, T., Menon, R. and Ciantar, E. (2021) 'Trauma during pregnancy', BJA education, 21(1), pp. 10–19. Available at: https://doi.org/10.1016/j.bjae.2020.08.005.

Kho, G.S. and Abdullah, J.M. (2018) 'Management of Severe Traumatic Brain Injury in Pregnancy: A Body with Two Lives', The Malaysian journal of medical sciences, 25(5), pp. 151–157. Available at: https://doi.org/10.21315/mjms2018.25.5.14.

Knight, M., Bunch, K., Kenyon, S., Tuffnell, D. and Kurinczuk, J.J. (2020) 'A national population-based cohort study to investigate inequalities in maternal mortality in the United Kingdom, 2009-17', Paediatric and perinatal epidemiology, 34(4), pp. 392–398. Available at: https://doi.org/10.1111/ppe.12640.

Korhonen, A., Verho, L., Aarnio, K., Rantanen, K., Saaros, A., Laivuori, H., Gissler, M., Tikkanen, M. and Ijäs, P. (2023) 'Subarachnoid Hemorrhage During Pregnancy and Puerperium: A Population-Based Study', Stroke (1970), 54(1), pp. 198–207. Available at: https://doi.org/10.1161/STROKEAHA.122.039235.

Kovach, M. (2015). Emerging from the margins: Indigenous methodologies. Research as resistance: Revisiting critical, Indigenous, and anti-oppressive approaches, 2, 43-64.https://books.google.co.ke/books?hl=en&lr=&id=4UNVCgAAQBAJ&oi

Leonard, S.A., Main, E.K. and Carmichael, S.L. (2019) 'The contribution of maternal characteristics and cesarean delivery to an increasing trend of severe maternal morbidity', BMC pregnancy and childbirth, 19(1), pp. 16–16. Available at: https://doi.org/10.1186/s12884-018-2169-3.

Lolk, K., Dreier, J.W., Sun, Y. and Christensen, J. (2022) 'Perinatal adversities and risk of epilepsy after traumatic brain injury: A Danish nationwide cohort study', Acta neurologica Scandinavica, 145(6), pp. 721–729. Available at: https://doi.org/10.1111/ane.13605.

MacDonald, E.J., Lepine, S., Pledger, M., Geller, S.E., Lawton, B. and Stone, P. (2019) 'Pre-eclampsia causing severe maternal morbidity – A national retrospective review of preventability and opportunities for improved care', Australian & New Zealand journal of obstetrics & gynaecology, 59(6), pp. 825–830. Available at: https://doi.org/10.1111/ajo.12971.

Maher, G.M., McCarthy, F.P., McCarthy, C.M., Kenny, L.C., Kearney, P.M., Khashan, A.S. and O'Keeffe, G.W. (2019) 'A perspective on pre-eclampsia and neurodevelopmental outcomes in the offspring: Does maternal inflammation play a role?', International journal of developmental neuroscience, 77(1), pp. 69–76. Available at: https://doi.org/10.1016/j.ijdevneu.2018.10.004.

Menon, R., & Irving, T. (2022). Trauma in Pregnancy. Textbook of Acute Trauma Care, 691-704.https://doi.org/10.1007/978-3-030-83628-3_35.

Miller, E. C., Schalekamp-Timmermans, S., Cipolla, M. J., & Staff, A. C. (2022). Cerebrovascular Pathophysiology in Preeclampsia and Eclampsia. In Chesley's Hypertensive Disorders in Pregnancy (pp. 265-288). Academic Press.https://doi.org/10.1016/B978-0-12-818417-2.00008-7.

Mol, B.W.J., Roberts, C.T., Thangaratinam, S., Magee, L.A., de Groot, C.J.M. and Hofmeyr, G.J. (2016) 'Pre-eclampsia', The Lancet (British edition), 387(10022), pp. 999–1011. Available at: https://doi.org/10.1016/S0140-6736(15)00070-7.

Narisawa, A., Nonaka, M., Akutsu, N., Kato, M., Harada, A. and Park, Y.-S. (2022) 'Unexplained mechanism of subdural hematoma with convulsion suggests nonaccidental head trauma: A multicenter, retrospective study by the Japanese Head injury of Infants and Toddlers study (J-HITs) group', PloS one, 17(11), pp. e0277103–e0277103. Available at: https://doi.org/10.1371/journal.pone.0277103.

Ndwiga, C., Odwe, G., Pooja, S., Ogutu, O., Osoti, A., E. Warren, C. and Spradley, F.T. (2020) 'Clinical presentation and outcomes of pre-eclampsia and eclampsia at a national hospital, Kenya: A retrospective cohort study', PloS one, 15(6), pp. e0233323–e0233323. Available at: https://doi.org/10.1371/journal.pone.0233323.

Neuendorf, K.A. (2019) 'Content analysis and thematic analysis', in Advanced Research Methods for Applied Psychology. 1st edn. Routledge, pp. 211–223. Available at: https://doi.org/10.4324/9781315517971-21.

Newman, M., & Gough, D. (2020). Systematic reviews in educational research: Methodology, perspectives and application. Systematic reviews in educational research: Methodology, perspectives and application, 3-22.https://doi.org/10.1007/978-3-658-27602-7_1.

Nyfløt, L.T., Sandven, I., Stray-Pedersen, B., Pettersen, S., Al-Zirqi, I., Rosenberg, M., Jacobsen, A.F. and Vangen, S. (2017) 'Risk factors for severe postpartum hemorrhage: a case-control study', BMC pregnancy and childbirth, 17(1), pp. 17–17. Available at: https://doi.org/10.1186/s12884-016-1217-0.

Ormesher, L., Higson, S., Vause, S., Clarke, B., Roberts, A., Johnstone, E. and Myers, J. (2019) 'Is pre-pregnancy cardiac dysfunction a risk factor for the development of pre-eclampsia?',

Pregnancy hypertension, 17, pp. S22–S22. Available at: https://doi.org/10.1016/j.preghy.2019.08.135.

Pandey, P., & Pandey, M. M. (2021). Research methodology tools and techniques. Bridge Center.ISBN 978-606-93502-7-0.

Patel, M., & Patel, N. (2019). Exploring Research Methodology. International Journal of Research and Review, 6(3), 48-55.E-ISSN: 2349-9788; P-ISSN: 2454-2237.

Quintao, C., Andrade, P. and Almeida, F. (2020) 'How to Improve the Validity and Reliability of a Case Study Approach', Journal of interdisciplinary studies in education, 9(2), p. 264. https://doi.org/10.32674/jise.v9i2.2026.

Rahman, M.S. (2016) 'The Advantages and Disadvantages of Using Qualitative and Quantitative Approaches and Methods in Language "Testing and Assessment" Research: A Literature Review', Journal of education and learning, 6(1), p. 102–. Available at: https://doi.org/10.5539/jel.v6n1p102.

Safdari, M., Safdari, Z. and Pishjoo, M. (2018) 'Intrauterine Fetal Traumatic Brain Injury Following Motor Vehicle Accident; A Case Report and Review of the Literature', Bulletin of emergency & trauma, 6(4), pp. 372–375. Available at: https://doi.org/10.29252/beat-060417.

Sardar Weli (2020) 'Determination of Factors Associated with Low Birth Weight among Babies Born in Sulaimania City, Kurdistan-Iraq', Journal of the Faculty of Medicine, Baghdad, 62(3). Available at: https://doi.org/10.32007/jfacmedbagdad.6231751.

Shoopala, H.M. and Hall, D.R. (2019) 'Re-evaluation of abruptio placentae and other maternal complications during expectant management of early onset pre-eclampsia', Pregnancy hypertension, 16, pp. 38–41. Available at: https://doi.org/10.1016/j.preghy.2019.02.008.

Singh, A., Kour, A., & Santpur, U. S. (2020). Acute Head Injury with Pregnancy. Indian Journal of Public Health Research & Development, 11(1), 1705-1709.https://doi.org/10.37506/ijphrd.v11i1.1217.

Spaite, D.W., Bobrow, B., Gaither, J.B., Keim, S.M., Barnhart, B.J., Chikani, V., Denninghoff, K., Mullins, T., Adelson, D., Rice, A.D., Viscusi, C. and Hu, C. (2019) 'Abstract 320: Statewide Implementation of the Prehospital Traumatic Brain Injury Guidelines in Children: The EPIC4Kids Study', Circulation (New York, N.Y.), 140(Suppl_2). Available at: https://doi.org/10.1161/circ.140.suppl_2.320.

Tantillo, G.B., Jetté, N., Yoo, J.Y., Stone, J., Egerman, M. and Dhamoon, M.S. (2020) 'Pregnancy-related complications and risk of postpartum readmission for seizures and epilepsy: A national study', Epilepsia (Copenhagen), 61(9), pp. 1990–1998. Available at: https://doi.org/10.1111/epi.16641.

Tochio, A., Obata, S., Saigusa, Y., Shindo, R., Miyagi, E. and Aoki, S. (2019) 'Does pre-eclampsia without proteinuria lead to different pregnancy outcomes than pre-eclampsia with proteinuria?', The journal of obstetrics and gynaecology research, 45(8), pp. 1576–1583. Available at: https://doi.org/10.1111/jog.14017.

Tran, P.L., Robillard, P.-Y., Dumont, C., Schweizer, C., Omarjee, A., Iacobelli, S. and Boukerrou, M. (2019) 'Recurrent or first preeclampsia in multiparae: A case-control study of

singleton pregnancies in Reunion Island', European journal of obstetrics & gynecology and reproductive biology, 240, pp. 80–86. Available at: https://doi.org/10.1016/j.ejogrb.2019.06.013.

Vaajala, M., Kuitunen, I., Nyrhi, L., Ponkilainen, V., Kekki, M., Huttunen, T.T. and Mattila, V.M. (2022) 'Birth rate after major trauma in fertile-aged women: a nationwide population-based cohort study in Finland', Reproductive health, 19(1), pp. 73–73. Available at: https://doi.org/10.1186/s12978-022-01387-w.

Valencia-Ortega, J., Saucedo, R., Peña-Cano, M.I., Hernández-Valencia, M. and Cruz-Durán, J.G. (2020) 'Immune tolerance at the maternal-placental interface in healthy pregnancy and pre-eclampsia', The journal of obstetrics and gynaecology research, 46(7), pp. 1067–1076. Available at: https://doi.org/10.1111/jog.14309.

Vigil, F.A., Bozdemir, E., Bugay, V., Chun, S.H., Hobbs, M., Sanchez, I., Hastings, S.D., Veraza, R.J., Holstein, D.M., Sprague, S.M., M Carver, C., Cavazos, J.E., Brenner, R., Lechleiter, J.D. and Shapiro, M.S. (2020) 'Prevention of brain damage after traumatic brain injury by pharmacological enhancement of KCNQ (Kv7, "M-type") K+ currents in neurons', Journal of cerebral blood flow and metabolism, 40(6), pp. 1256–1273. Available at: https://doi.org/10.1177/0271678X19857818.

Voorhees, H.L. and Howell Smith, M.C. (2020) 'Qualitative and Quantitative Method Integration in Diabetes Communication Research: Applications and Contributions', Qualitative health research, 30(2), pp. 228–235. Available at: https://doi.org/10.1177/1049732319868985.

Wosenu, L., Worku, A.G., Teshome, D.F. and Gelagay, A.A. (2018) 'Determinants of birth asphyxia among live birth newborns in University of Gondar referral hospital, northwest

Ethiopia: A case-control study', PloS one, 13(9), pp. e0203763–e0203763. Available at: https://doi.org/10.1371/journal.pone.0203763.

Wu, C.-L., Kor, C.-T., Chiu, P.-F., Tsai, C.-C., Lian, I.-B., Yang, T.-H., Tarng, D.-C. and Chang, C.-C. (2017) 'Long-term renal outcomes in patients with traumatic brain injury: A nationwide population-based cohort study', PloS one, 12(2), pp. e0171999–e0171999. Available at: https://doi.org/10.1371/journal.pone.0171999.

Young, M.F., Oaks, B.M., Tandon, S., Martorell, R., Dewey, K.G. and Wendt, A.S. (2019) 'Maternal hemoglobin concentrations across pregnancy and maternal and child health: a systematic review and meta-analysis', Annals of the New York Academy of Sciences, 1450(1), pp. 47–68. Available at: https://doi.org/10.1111/nyas.14093.

Zhang, C., Gong, Y., & Brown, S. (2023). Research methodology. In Blockchain Applications in Food Supply Chain Management: Case Studies and Implications (pp. 77-98). Cham: Springer Nature Switzerland.https://doi.org/10.1007/978-3-031-27054-3_3.