A REVIEW ON MATERNAL AND PERINATAL OUTCOME OF ABRUPTIO PLACENTA IN HOSPITAL UNIVERSITI SAINS MALAYSIA, KELANTAN

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List of Abbreviations

O&G	Obstetrics and Gynaecology
USM	Universiti Sains Malaysia
HUSM	Hospital Universiti Sains Malaysia
BMI	Body Mass Index
NICU	Neonatal Intensive Care Unit
PPH	Postpartum haemorrhage
DIVC	Disseminated intravascular coagulatopathy
ICU	Intensive Care Unit
LSCS	Lower segment caesarean section
SVD	Spontaneous vertex delivery
ABD	Assisted breech delivery
VAD	Vacuum assisted delivery
MSB	Macerated stillbirth
FSB	Fresh stillbirth
SPSS	Statistical Package for the Social Sciences
JEPeM	Human Research and Ethics Committee USM

ABSTRAK

Latar belakang:

Abruptio placenta adalah komplikasi semasa kehamilan di mana berlaku pemisahan uri dari dinding rahim sebelum bermulanya proses kelahiran bayi. Ia menyebabkan kadar morbiditi dan kematian yang tinggi kepada bayi dan ibu mengandung. Tujuan kajian ini ialah untuk mengenalpasti factor-faktor risiko *abruptio placenta* serta kesan-kesannya kepada ibu dan bayi.

Kaedah Kajian:

Kajian retrospektif ini melibatkan ibu-ibu mengandung yang didiagnos dengan *abruptio placenta* dan melahirkan di Hospital Universiti Sains Malaysia, Kubang Kerian, Kelantan pada Januari 2008 sehingga Disember 2020. Terdapat sebanyak 288 pesakit yang didiagnos dengan abruptio placenta selama tempoh tersebut dan kami telah menggunakan kaedah persampilan secara rawak yang sistematik bagi memilih 150 pesakit untuk kajian ini. Kedah yang sama juga diaplikasikan bagi memilih 150 pesakit yang tidak didiagnos dengan *abruptio placenta* bagi membuat perbandingan. Data sosio-demografik, factor-faktor risiko, komplikasi kepada ibu dan bayi direkod dan dianalisa.

Keputusan:

Jumlah kes *abruptio placenta* dalam kajian ini adalah sebanyak 288 kes daripada 103,042 jumlah kelahiran (0.3%). Untuk faktor risiko, pesakit yang mempunyai *pre-eclampsia* (adj OR 4.656, 95% CI 2.214-9.789, p<0.001), *PPROM* (adj OR 5.377, 95% CI 1.854-15.596, p =0.002) dan sejarah urutan perut tradisional (adj OR 10.491. 95% CI 1.188-92.636, p =0.034) membawa risiko lebih tinggi kepada abruptio placenta. Kadar kelahiran secara *caeserean section* didapati lebih tinggi direkodkan pada kumpulan *abruptio placenta* (66.7%) berbanding

dengan kumpulan *non-abruptio placenta* (29.3%) (p<0.001). Dalam kajian ini, kejadian tumpah darah, *DIVC* dan transfusi darah berhubung kait dengan abruptio placenta. Untuk kesan terhadap bayi, pesakit yang didiagnos dengan *abruptio placenta* mempunyai kadar kelahiran bayi pramatang yang tinggi iaitu sebanyak 107 kes (71.3%) (p<0.001). Baby pada kumpulan *abruptio placenta* mempunyai kadar kemasukan ke unit rawatan rapi bayi (p<0.001), skor Apgar kurang dari tujuh dalam lima minit (p<0.001) dan kelahiran mati (p<0.001) yang lebih tinggi berbanding kumpulan *non-abruptio placenta*.

Kesimpulan:

Kajian ini menunjukkan penyakit *pre-eclampsia*, *PPROM* dan urutan perut tradisional membawa risiko kepada *abruptio placenta*. Terdapat beberapa hubungkait di antara komplikasi *abruptio placenta* kepada ibu (kejadian tumpah darah selepas kelahiran, *DIVC*, transfusi darah dan kemasukan ke unit rawatan rapi) dan bayi (kelahiran pramatang, kemasukan bayi ke unit rawatan rapi, skor Apgar yang rendah dan kelahiran mati).

Abstract

Background:

Abruptio placenta is one of the most common etiologies of antepartum hemorrhage. Because of its detrimental feto-maternal effect, this study aimed to identify the risk factors, maternal and neonatal outcomes of abruptio placenta by comparing them with cases without abruptio placenta who delivered within the same years.

Methodology:

This was a 13-year retrospective case-control study of abruptio placenta in Hospital Universiti Sains Malaysia, Kubang Kerian, Kelantan in January 2008 until December 2020. Out of 288 cases of abruptio placenta recorded, only 223 cases fulfilled the inclusion and exclusion criteria. Systemic random sampling method was applied to recruit 150 cases of abruptio placenta and another 150 cases of non-abruptio placenta cases. The sociodemographic data, maternal and neonatal outcomes were recorded and analysed using SPSS version 27.

Results:

The incidence of abruptio placenta in our study is 288 cases out 103,042 of deliveries (0.3%). As for the risk factors, patients with pre-eclampsia (adj OR 4.656, 95% CI 2.214-9.789, p<0.001), PPROM (adj OR 5.377, 95% CI 1.854-15.596, p=0.002) and history of abdominal massage (adj OR 10.491. 95% CI 1.188-92.636, p=0.034) had significant increased risk for abruptio placenta. In term of pregnancy outcome, the caesarean section rate was higher in the abruptio placenta group as compared to non-abruptio placenta cases (p<0.001). These correlate with the severity of abruptio placenta cases in which 70 (46.7%) were in grade 2 abruptio placenta and 11 (7.3%) were in grade 3 group. In this study, the incidence of PPH was higher in the abruptio placenta group 81 (54.0%) whereas only 31 cases (20.7%) in the control group

(p<0.001). 10 (6.7%) patients in the abruptio placenta group had DIVC as compared to only one (0.7%) case in the non-abruptio group (p=0.006). There were 54 cases (36.0%) that required blood transfusion in the abruptio placenta group and 15 cases (10.0%) in the non-abruptio placenta cases (p<0.001). 16 (10.7%) of abruptio placenta cases required ICU admission whereas there were only four (2.7%) cases in the control group (p=0.005). As for the perinatal outcome, high rate of preterm deliveries was observed in the abruptio placenta group (p<0.001). Newborn in the abruptio placenta group had higher rate of NICU admission (p<0.001), Apgar score less than 7 in 5 minute (p<0.001) and stillbirth (p<0.001) as compared to the control group. There were four cases of early neonatal death in the abruptio placenta group in this study p=0.176.

Conclusion:

This study showed that pre-eclampsia, PPROM and history of abdominal massage are significant risk factors of abruptio placenta. There was statistically significant difference in the maternal complications (PPH, DIVC, blood transfusion and ICU admission) and perinatal outcome (prematurity, Apgar score less than 7 in 5 minute, NICU admission and stillbirth).

Keywords: *Abruptio placenta, incidence, risk factors, maternal outcomes, neonatal outcomes*

1.0 INTRODUCTION

Placental abruption (also referred to as abruptio placentae) is defined as partial or complete detachment of placenta prior to the delivery of fetus. It is a significant cause of both maternal morbidity and neonatal morbidity and mortality, particularly when it occurs preterm. Abruptio placentae complicates approximately 2 to 10 per 1000 births.(Ananth *et al*., 2015) In one large series of over 500 abruptions with a live birth, 60.4 percent occurred at term, 25.3 percent occurred at 32 to 36 weeks, and 14.3 percent occurred before 32 weeks (Tikkanen, 2011).

The clinical hallmarks of abruption include painful vaginal bleeding accompanied by tetanic uterine contractions, uterine hypertonicity and a non-reassuring fetal heart rate pattern (Li *et al*., 2019). Despite extensive research, the majority of cases of abruptio placentae continue to be of unknown etiology. However, there are several identified risk factors which include high parity, advanced maternal age, low socioeconomic status, cigarette smoking, abdominal trauma, alcohol use, maternal hypertension, polyhydramnios, multiple pregnancies, thrombophilia and prior history of abruption (Igwegbe AO, Eleje GU, 2013).

For the mother, the potential consequences of abruptio placenta are primarily related to the severity of the placenta separation, meanwhile the risks to the fetus are related to both the severity of the separation and the gestational age at which the delivery occurs. There may be no significant complications with mild placental separation. However, as the degree of the placental separation increases, the maternal and neonatal adverse outcome also increase (Sheiner *et al*., 2002).

Good maternal outcome is dependent on the holistic management of hemodynamic status and the renal status of the patient. As compared to pregnancies without placenta

abruption, the perinatal mortality with abruptio placenta is approximately 20-fold higher (Dutta *et al*., 2015). This is related to the severity of the abruption, misdiagnosis and delay in commencement of treatment.

Because of the possible detrimental feto-maternal effect of abruptio placenta, we conducted this study to evaluate its prevalence and associated factors. Clinicians may provide extra caution in managing patients in the presence of these factors.

2.0 LITERATURE REVIEW

2.1 Prevalence of Abruptio Placenta

A retrospective study in tertiary hospital in Kelantan, Malaysia showed that abruptio placenta complicates approximately 0.4 to 1.0% of pregnancies (Norhayati *et al*., 2016). A study of abruptio placenta done in Hospital Universiti Sains Malaysia (HUSM) revealed that the incidence of abruptio placenta in this hospital was 0.5% (Zanariah., 1997). There was lack of published study on abruptio placenta done in Asia particularly Southeast Asia, however a retrospective study conducted in Thailand found that there were 103 cases of abruptio placenta among 111,375 singleton deliveries (0.92 in 1,000) over a 15-year period (Pitaphrom and Sukcharoen, 2006). A study in Taiwan showed that the incidence of abruptio placenta was 9 per 1000 singleton pregnancies (Hung et al., 2007). Another study conducted in Netherlands documented a prevalence of 0.2% (Ruiter *et al*., 2015). Most studies held in India showed that prevalence of abruptio placenta ranges from 0.5-0.8%. Meanwhile, a study conducted in United State showed a higher prevalence of 9.6/1000 with severe abruptio placenta accounting for 6.5/1000 (Ananth *et al*., 2016).

2.2 Pathophysiology of Abruptio Placenta

Abruptio placenta is initiated by haemorrhage into the decidua basalis. The accumulating blood splits the decidua, leaving a thin layer adhered to the myometrium. Consequently, a decidual haematoma forms and expands to cause separation and compression of the adjacent placenta.

It likely begins with rupture of a decidual spiral artery and then expanding retroplacental haematoma. In the early stages of abruptio placenta, there may be absence of

clinical manifestation. Even with continued bleeding and placental separation, abruptio placenta can still be either total or partial. With either, bleeding typically insinuates itself between the membranes and uterus, subsequently escaping through the cervix to cause revealed haemorrhage.

Less often, the blood is retained between the detached placenta and the uterus, leading to concealed haemorrhage and delayed diagnosis. This delay results in greater maternal and fetal hazards. Apart from that, in concealed haemorrhage, the probability of consumptive coagulopathy is raised. This is because increased pressure within the intervillous space, caused by the expanding retroplacental clot, forces more placenta thromboplastin into the maternal circulation (Cunningham et al., 2018).

Four grades of abruptio placenta have been described based on the clinical findings. Grade 0 is the asymptomatic group, whereby diagnosis is usually made retrospectively by presence retroplacental clot detected post-delivery. In grade 1 (mild), there may be a small amount of per vaginal bleeding and slight uterine tenderness however there is no sign of maternal and fetal distress. It occurs in 40.0% of cases. Patients with grade 2 (moderate) abruptio placenta may present with moderate amount of vaginal bleeding and significant uterine tenderness as well as evidence of fetal distress, however there is no sign of maternal shock yet. 45.0% of women will present with grade 2 abruptio placenta. Grade 3 (severe) abruptio placenta has heavy vaginal bleeding or concealed bleeding with tetanic uterus or board-like rigidity on palpation associated with maternal shock and often coagulopathy and fetal death. This is found in 15.0% of cases (Tikkanen, 2010).

2.3 Risk Factors of Abruptio Placenta

The aetiology of bleeding at decidua basalis remains unknown in most cases, despite ample clinical and epidemiologic research. A previous study of abruptio placenta done in HUSM showed that maternal age above 35 years and increasing parity had significant association with abruption. Apart from that, the commonest predisposing factors were hypertension (30.3%) and traditional abdominal massage (25.4%). Furthermore, the study found that among the hypertensive patients, eclampsia had the highest incidence of abruptio placenta (Zanariah., 1997). Similar findings were documented by a retrospective study done in Taiwan in which increasing parity and age of more than 35 years were at higher risk to develop abruptio placenta (Hung et al., 2007).

On the contrary, a study in Thailand found that majority of the abruptio placenta cases were among the age of 20-24 (31.1%), followed by 25-29 years (23.3%), 30-34 years (18.4%) and more than 35 years (15.5%). Apart from that, most of the patients were primigravida (52.4%) and there was only 2.0% of patients with parity more than 4. The study also showed that 30.1% of patients had gestational hypertension, in which 17.5% of them had severe pre-eclampsia and 11.7% had mild pre-eclampsia (Pitaphrom and Sukcharoen, 2006)

A study conducted in India documented that the incidence of abruptio placenta is more common in age group of 20 to 25 years old (36.0%). They also demonstrated that the incidence of placenta abruption increased with increasing parity (Abirami *et al*., 2020). In contrast, another study done in the same country showed that the maximum number of cases (40.0%) of abruptio placenta were between 30-35 years old. The study also concluded that majority of cases were gravida 2, comprises of 35% followed by gravida 3 (30.0%), gravida 4,5 (20.0%) and gravida 1(15.0%) (Mishra and Misra, 2019).

A study conducted in Singapore which studied 93 cases of pre-eclampsia demonstrated that 2 (2.0%) of the patients had abruptio placenta (Loi et al., 2007). Another study done in Israel demonstrated that hypertensive disease in pregnancy constitutes 15.3% of patients with abruptio placenta (Pariente *et al*., 2011). A study done in India concluded that abruptio placenta is more common among patients with severe pre-eclampsia than who were normotensive, in which there was 67.0% of patients with severe pre-eclampsia, followed by 8.6% and 7.0% with eclampsia and chronic hypertension respectively. They also mentioned that even normotensive groups had abruptio placenta which was about 17.4% (Sengodan and Dhanapal, 2017).

An article in the Tropical Journal of Obstetrics and Gynaecology which studied the prevalence, risk factors and outcome of abruptio placenta in Nigeria showed hypertensive disorder of pregnancy contributed to 53.1% of cases. Multiple pregnancies and polyhydramnios accounted for 8.0% and 6.0% of cases respectively, whilst other recognizable risk factors were trauma (4.0%), previous abruptio placenta (4.0%) and smoking (1.0%) (Akadri *et al*., 2018)

2.4 Mode of Delivery in Abruptio Placenta

A study done in HUSM demonstrated that majority of patients with abruptio placenta delivered vaginally (61.2%) in which 88.2% of them comprised of intrauterine death cases. The study also found that 38.8% delivered via caesarean section whereby 83.3% of the babies were born live and subsequently, 10.8% of them had early neonatal death (Zanariah., 1997). A study conducted in Nigeria concluded that 63.3% cases of abruptio placenta underwent emergency caesarean section, whereby most of them were done on account of abruptio placenta with live fetus (Akadri *et al*., 2018).

As compared to a 3-year review in India, the incidence of caesarean section was only 27.1% whereby the most common indication was for fetal distress. Majority of the patients in this study had grade 2 abruption and most of their patients successfully delivered vaginally following induced labour (Mohapatra and Thanikkal, 2020). This discrepancy in the mode of delivery is largely due to the fetal status at the time of the diagnosis of abruptio placenta, in which in a situation where there is live fetus in distress, emergency caesarean section is mandatory. On the contrary, patients who were confirmed to have intrauterine death were allowed to have vaginal delivery provided there is absence of obstetrics indications for caesarean section such as transverse lie or maternal complications.

2.5 Maternal Outcome of Abruptio Placenta

A retrospective study of abruptio placenta in HUSM demonstrated that postpartum hemorrhage (PPH) and disseminated intravascular coagulation (DIVC) were the two commonest complications, occurring in 37.3% and 34.3% of cases respectively. Other complications included hypovolemic shock (16.4%) and acute renal failure (1.5%). Fortunately, there was no maternal mortality in the study (Zanariah., 1997).

A study on pregnancy outcome of abruptio placenta in Thailand found that 19.4% of patients developed hemorrhagic shock and 5.8% had DIVC (Pitaphrom and Sukcharoen, 2006). Another study in India showed that major maternal morbidity attributed to abruptio placenta was PPH, constituting 35.0%, followed by shock (15.0%), sepsis (12.9%), DIVC (8.6%) and renal failure (5.0%). The study demonstrated that 0.7% of patients underwent emergency hysterectomy with 5.2% of cases of maternal mortality (Mohapatra and Thanikkal, 2020).

Another study conducted in India showed that PPH accounts for 8.5% in grade 1 cases, 22.0% in grade 2 and 100.0% in grade 3 cases, whereas other complications are maternal blood transfusion (14.9%), maternal sepsis (0.3%) and hysterectomy (0.4%) (Pariente *et al*., 2011)

An article in International Journal of Reproduction, Contraception, Obstetrics and Gynaecology in 2019 studied the maternal and fetal outcome of abruptio placenta concluded that PPH is the commonest complication of abruptio placenta, constituting 21.0% of cases (Sambath *et al*., 2019). A study conducted in Nigeria showed that 34.7% of cases had PPH in which 81.6% of them required blood transfusion. 8.2% of their patients required hysterectomy and there was 4.1% of maternal mortality (Akadri *et al.,* 2018)

2.6 Perinatal Outcome of Abruptio Placenta

The fetal complications of abruptio placenta in a previous study in HUSM found that acute fetal distress and intrauterine death were the two commonest complications, accounting for 44.3% and 54.7% of cases respectively (Zanariah.,1997). A retrospective study done in Indonesia which studied the effect of maternal disease and antepartum hemorrhage on asphyxia revealed that 73.5% of mothers with abruptio placenta delivered baby with perinatal asphyxia (Sumarni et al., 2022). Another study in Thailand demonstrated that 30.1% of abruptio placenta cases had poor perinatal outcomes which included perinatal asphyxia, stillbirth and early neonatal death (Pitaphrom and Sukcharoen, 2006).

An article in the Annals of International Medical and Dental Research which studied cases of abruptio placenta for a two-year period in India demonstrated that majority of the birth weight of babies born as a consequence of abruptio placenta ranges from 2000-2499g accounting for 32.87% of cases, followed by 1500-1999g, constituting 30.07% of cases. This study also showed 27.87% of babies required Neonatal Intensive Care Unit (NICU) admission (Mohapatra and Thanikkal, 2020).

Another study done in India which categorize NICU admission based on severity of abruptio placenta showed that there was 20% of babies in grade 1 group required admission, 50% of babies in grade 0, 83.3% of cases among grade 2 and there was 0% of NICU admission in grade 3. They also demonstrated that neonatal morbidity was higher in the group that had vaginal delivery as compared to caesarean section, whereby 66% of babies born via vaginal deliveries required NICU admission as compared to 31.3% in caesarean section (Tambawaala and Kale, 2019).

A retrospective study in Israel which studied labour complications and birth outcome in preterm deliveries complicated with abruptio placenta concluded that 21% of babies were born with Apgar score less than 7 in 5 minutes. This study also showed that 13.3% had macerated stillbirth (MSB) , 3.3% had fresh stillbirth (FSB) and 13.3% had early neonatal death (Sheiner *et al*., 2002). A study in Tanzania demonstrated that 20% of babies born as a consequence of abruptio placenta had fetal distress, 21% was born with Apgar score less than 7 in 5 minutes, 34.7% was stillbirth and 23.2% had early neonatal death (Nandonde *et al*., 2016).

A study on the risk factors for placental abruption in Taiwan concluded that 14.5% of patients with abruptio placenta delivered baby with Apgar score less than 7 in 5 minutes of life, 24.7% was admitted to NICU and 6% had stillbirth (Hung *et al*., 2007).

A study on maternal and fetal outcome of abruptio placenta in India demonstrated that 28% cases of abruptio placenta was complicated with stillbirth and 10% cases of early neonatal death, mainly due to prematurity and growth restriction (Sambath *et al*., 2019). On the contrary, a retrospective cohort study conducted by Ananth C.V et al in 1999 showed that there was 5.3% of cases of stillbirth associated with abruptio placenta (Ananth *et al*., 1999).

3.0 JUSTIFICATION OF STUDY

The latest study conducted about abruptio placenta in HUSM was in 1997, which was 24 years ago. As abruptio placenta is associated with significant maternal and perinatal morbidity and mortality, it is important to know the general indices, risk factors and outcome of this disease.

This study is carried out to provide the latest local data on the risk factors contributing to abruptio placenta and its maternal and perinatal outcome. It is hoped that this study will help in recognizing certain risk factors which may assist in managing patients and minimize the feto-maternal morbidity and mortality, hence improving patient's outcome. Apart from that, data obtained from this study can be used for meta-analysis on abruptio placenta which will provide a more accurate results, therefore providing more significant intervention in managing patients having the risk factors of abruptio placenta.

4.0 RESEARCH QUESTIONS

4.0.1 What are the risk factors associated with abruptio placenta in HUSM?

4.0.2 What is the maternal and neonatal outcome of abruptio placenta in HUSM?

5.0 OBJECTIVES

5.1 General Objectives

To study the maternal and perinatal outcome of patients with abruptio placenta in HUSM from year 2008 until 2020.

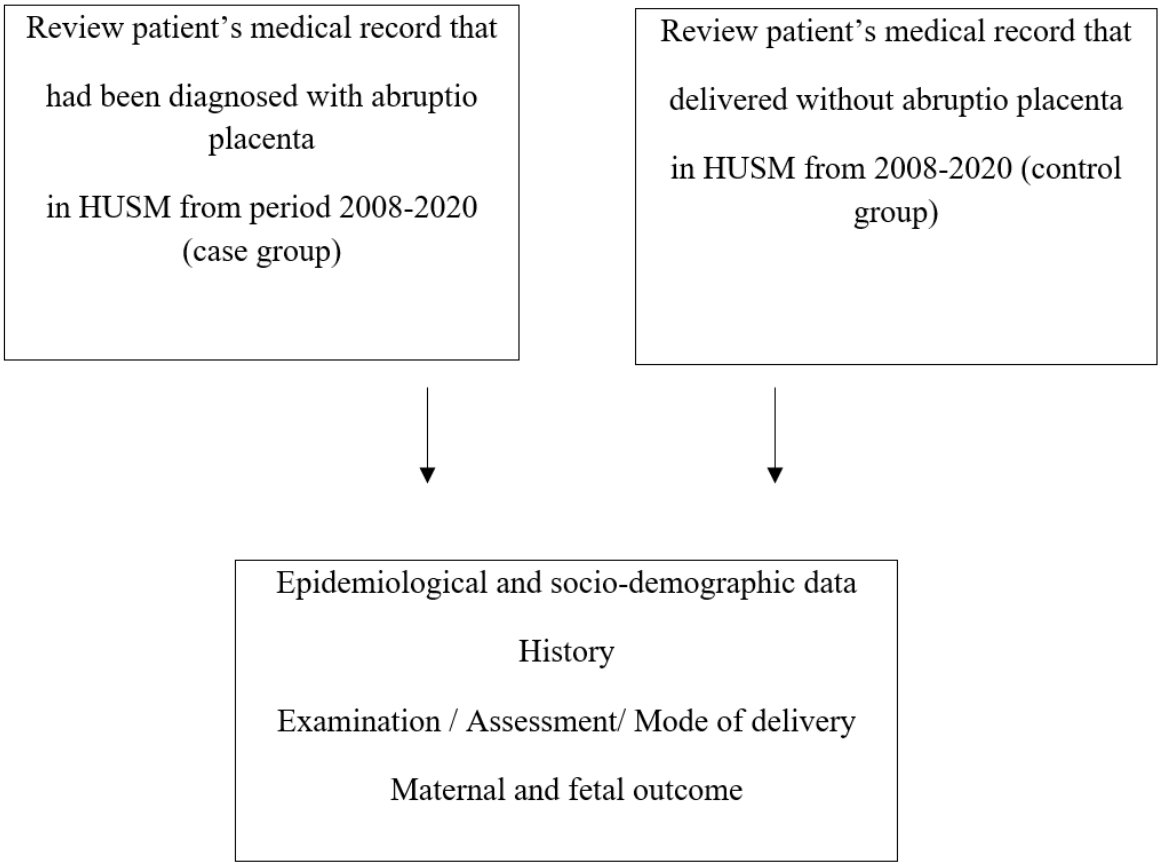
5.2 Specific Objectives

4.3.1 To identify the risk factors of abruptio placenta in HUSM

4.3.2 To compare the maternal and neonatal outcome of abruptio placenta with non-abruptio placenta cases in HUSM

6.0 RESEARCH METHODOLOGY

6.1 Conceptual Framework



6.2 Study Design and Area

This is a retrospective case-control study which was conducted at Department of Obstetrics and Gynaecology (O&G) of HUSM. It is a tertiary centre located in Kubang Kerian, Kelantan which is the referral centres for cases from districts of Kubang Kerian, Pasir Puteh, Bachok and Besut, Terengganu.

The Department of O&G comprises of two antenatal wards, one postnatal ward, one gynaecology ward and one labour room. There is a separate operation theatre situated in the labour room exclusively functions to run the cases for labour ward or antenatal ward cases

during working hours. A well-equipped separate room is also available in the labour room for resuscitation of newborns.

6.3 Reference Population

For the case group, it included all pregnant women who were admitted to HUSM for delivery and were diagnosed with abruptio placenta prior to delivery.

As for the control group, it included all pregnant women who were admitted to HUSM for delivery and were not diagnosed with abruptio placenta prior to delivery.

6.4 Source Population

Pregnant women who were diagnosed with abruptio placenta in HUSM, Kubang Kerian

6.5 Study Population

Pregnant women who were diagnosed with abruptio placenta in HUSM, Kubang Kerian, Kelantan from year 2008 until 2020 and fulfilled the inclusion and exclusion criteria

6.6 Subject Criteria

All pregnant women who were diagnosed with abruptio placenta and delivered in HUSM fulfilling below criteria were included in this study:

- 24 weeks and above gestation
- Singleton pregnancy
- Diagnosed with abruptio placenta (in case group)

Women with the following criteria were excluded from the study:

- Placenta praevia
- Local trauma of the lower genital tract
- Indeterminate antepartum haemorrhage
- Vasa praevia

6.7 Sample Size Calculation

The sample size was calculated using Sample Size Calculator version 2.0 (Ariffin, W.N., 2017) for each of the objectives.

Sample size was determined using a two-proportion formula.

P_0 = proportion of risk factor among control cases (non-disease)

P_1 = proportion of risk factor among cases (abruptio placenta cases)

Significance level: 0.05(Two-tailed)

Power: 80%

Drop-out rate: 20%

Table 6.1: Risk factors

No.	Risk factor	P_0	P_1	n	(nx2) + 20%	Reference
1.	Age <35 year-old	0.85	0.3	19	46	Hung TH et al (2007)
2.	Parity <4	0.97	0.52	14	33	Hung TH et al (2007)
1.	Hypertension	0.016	0.153	64	150	Sheiner E et al (2002)
2.	Multiple pregnancy	0.99	0.8	50	120	Akadri AA et al (2018)
3.	Polyhydramnios	0.98	0.6	22	53	Akadri AA et al (2018)
4.	Trauma	0.75	0.4	39	94	Akadri AA et al (2018)
5.	Previous history of abruptio placenta	0.99	0.4	12	29	Akadri AA et al (2018)

Table 6.2: Maternal Outcome

No.	Maternal outcome	P_0	P_1	n	(nx2) + 20%	Reference
1.	Postpartum hemorrhage	0.2	0.008	39	93	Pariente G et al (2010)
2.	Hemorrhagic shock	0.6	0.15	17	41	Mohapatra S et al (2020)
3.	Disseminated intravascular coagulopathy	0.63	0.085	11	26	Mohapatra S et al (2020)
4.	Acute renal failure	0.04	0.05	25	60	Mohapatra S et al (2020)
5.	Maternal mortality	0.893	0.517	28	67	Mohapatra S et al (2020)
6.	Hysterectomy	0.98	0.8	59	141	Tikkanen M et al (2011)

Table 6.3: Neonatal Outcome

No.	Neonatal outcome	P_0	P_1	n	(nx2) + 20%	Reference
1.	Low Apgar score at 5mins of life	0.025	0.7	7	17	Hung T.H. et al (2007)
2.	NICU admission	0.04	0.247	44	106	Hung T.H. et al (2007)
3.	Stillbirth	0.011	0.166	52	125	Sheiner E et al (2002)
4.	Early neonatal death	0.002	0.133	57	137	Sheiner E et al (2002)

The highest calculated sample size among all the objectives was 150, hence a minimum of patients required to be recruited to meet 80% of statistical power in this study were 150 for each criteria. Total number of sample size for this study is 300 patients.

6.8 Ethical Considerations

This study was conducted after obtaining ethical approval from the Human Research Ethics Committee of USM (JEPeM).

Since it is a retrospective observational/non-interventional study, it did not interfere with the management of the patient during study. Hence, consent was only taken from the hospital director to review medical records of the patient without any disclosure of patients' details such as name or registration number. All data were collected as in the proforma using subject ID and was saved in soft copy in computer and protected with password. Data can only be reviewed by the principal investigator.

All the information obtained from this study will be kept confidential and only summarized data will be presented in reports or publications.

The principal investigator does not have any conflict of interest between the research topic and the study subjects.

6.9 Sampling Method and Subject Recruitment

Sample were patients who delivered in HUSM from 2008 until 2020. A total of 288 cases who were diagnosed with abruptio placenta were reviewed. From this, only 223 cases fulfilled the inclusion and exclusion criteria.

The data was traced through computer-generated list from medical record office as well as from labour room birth registry book. The patients were randomly selected using Simple Random Sampling Generator using Microsoft Excel Najib (2015). A total number of 150 abruptio placenta cases were recruited into this study. Patients with inadequate information were excluded.

Delivery record and other information required were extracted with aids of proforma/ data collection sheets. All the date were tabulated for data analysis.

6.10 Research Tool

Data collection sheet (proforma) was used and each patient had a dedicated sheet. The data collection sheet was divided into four sections:

i) Sociodemographic background

ii) Antenatal problems

iii) Maternal outcomes

iv) Neonatal outcomes

Information collected included maternal age, ethnicity, gravida, parity, gestational age at delivery, body mass index (BMI), antenatal problems such as hypertension and diabetes mellitus, duration of diagnosis of abruptio placenta until delivery of baby and the amount of retroplacental clots. The maternal outcomes section comprised of mode of delivery, estimated

blood loss and the associated complications of abruptio placenta such as PPH, hypovolemic shock, acute renal failure, coagulopathy and hysterectomy.

The fetal outcomes collected were birth weight, Apgar score in 1 and 5 minutes of life, NICU admission, intubation, stillbirth and early neonatal death.

6.11 Definitions of Operational Terms

Primary postpartum haemorrhage (PPH) is the loss of 500ml or more of blood from the genital tract within 24 hours of birth of a baby. PPH can be minor (500-1000ml) or major (more than 1000ml). Major could be divided to moderate (1000-2000ml) or severe (more than 2000ml). In this study, patient who undergoing caesarean section, EBL more than 1000ml were taken and patient whom normal delivery (SVD), EBL more than 500ml were taken (RCOG, 2016).

Disseminated intravascular coagulopathy (DIVC) is defined as systemic activation of blood coagulation, which results in generation and deposition of fibrin and formation of microvascular thrombi and activation of plasmin, eventually leading to multiple organ dysfunction. It is diagnosed when there is evidence of thrombocytopenia (less than $100X10^9$/L), prolongation of the prothrombin time (PT) more than 3 seconds and low level of fibrinogen (less than 1g/L) (ISTH DIC scoring, 2007).

Maternal mortality is the death of a woman from direct or indirect obstetric causes, during pregnancy and childbirth or within 42 days of termination of pregnancy, irrespective of the duration and site of pregnancy. (WHO, 2017)

Low Apgar score: Apgar score of less than 7 at 5 minutes of life (ACOG, 2014)

Stillbirth: A baby delivered with no signs of life known to have died, after 24 completed weeks of pregnancy (RCOG, 2010).

Early neonatal death is defined as a death among live births that occurred during the first 7 days of life (WHO, 2019)

Grades of abruptio placenta were as follows: (Tikkanen, 2010)

Grade 0 abruptio placenta: the asymptomatic group, whereby diagnosis was usually made retrospectively by presence retroplacental clot detected post-delivery.

Grade 1 (mild) abruptio placenta: presence of a small amount of per vaginal bleeding and slight uterine tenderness however there was no sign of maternal and fetal distress.

Grade 2 (moderate) abruptio placenta: presented with moderate amount of vaginal bleeding and significant uterine tenderness as well as evidence of fetal distress, however there was no sign of maternal shock yet.

Grade 3 (severe) abruptio placenta: had heavy vaginal bleeding or concealed bleeding with tetanic uterus or board-like rigidity on palpation associated with maternal shock and often coagulopathy and fetal death.

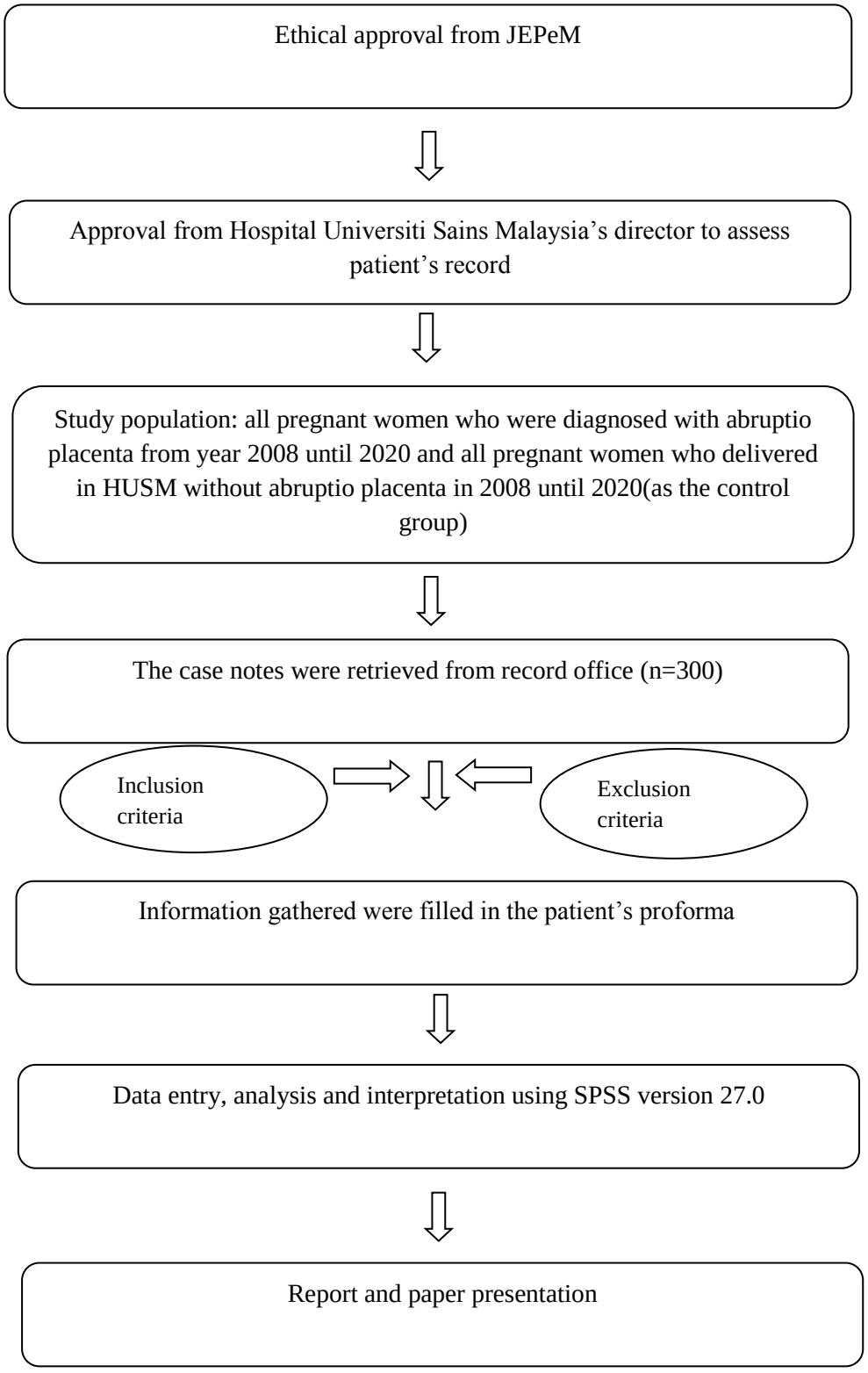
6.12 Statistical Analysis

Data entry and analysis was done using SPSS version 27.0. Descriptive analysis was used for socio-demographic characteristics and independent variables. Categorical variables were presented as frequency(n) and percentage (%).

Numerical data which is normally distributed was presented as mean and standard deviation. Pearson's Chi-square test and Fisher's exact test was used to identify the association of maternal and perinatal outcome between both groups. The p value was calculated for the pregnancy outcomes. The level of less than 0.05 ($P<0.05$) was considered statistically significant.

Simple Logistic Regression (SLR) tests were applied in the univariate analysis. Variables with p value less than 0.25 or clinically important in the univariate analysis were selected for the multivariate analysis. Forward, backward, and manual methods were used to determine our final model. Then, we used the Multiple Logistic Regression (MLR) test to analyse the multivariate analysis. All assumptions for the tests were met. Variables comparison with a p-value less than 0.05 is considered significant.

6.13 Study Flowchart



7.0 THE MANUSCRIPT

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A Review on Maternal and Perinatal Outcome of Abruptio Placenta in Hospital Universiti Sains Malaysia, Kelantan

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Abstract

Background:

Abruptio placenta is one of the most common etiologies of antepartum hemorrhage. Because of its detrimental feto-maternal effect, this study aimed to identify the risk factors, maternal and neonatal outcomes of abruptio placenta by comparing them with cases without abruptio placenta who delivered within the same years.

Methodology:

This was a 13-year retrospective case-control study of abruptio placenta in Hospital Universiti Sains Malaysia, Kubang Kerian, Kelantan in January 2008 until December 2020. Out of 288 cases of abruptio placenta recorded, only 223 cases fulfilled the inclusion and exclusion criteria. Systemic random sampling method was applied to recruit 150 cases of abruptio placenta and another 150 cases of non-abruptio placenta cases. The sociodemographic data, maternal and neonatal outcomes were recorded and analysed using SPSS version 27.

Results:

The incidence of abruptio placenta in our study is 288 cases out 103,042 of deliveries (0.3%). As for the risk factors, patients with pre-eclampsia (adj OR 4.656, 95% CI 2.214-9.789, p<0.001), PPROM (adj OR 5.377, 95% CI 1.854-15.596, p=0.002) and history of abdominal massage (adj OR 10.491. 95% CI 1.188-92.636, p=0.034) had significant increased risk for abruptio placenta. In term of pregnancy outcome, the caesarean section rate was higher in the abruptio placenta group as compared to non-abruptio placenta cases (p<0.001). These correlate with the severity of abruptio placenta cases in which 70 (46.7%) were in grade 2 abruptio placenta and 11 (7.3%) were in grade 3 group. In this study, the incidence of PPH was higher in the abruptio placenta group 81 (54.0%) whereas only 31 cases (20.7%) in the control group

(p<0.001). 10 (6.7%) patients in the abruptio placenta group had DIVC as compared to only one (0.7%) case in the non-abruptio group (p=0.006). There were 54 cases (36.0%) that required blood transfusion in the abruptio placenta group and 15 cases (10.0%) in the non-abruptio placenta cases (p<0.001). 16 (10.7%) of abruptio placenta cases required ICU admission whereas there were only four (2.7%) cases in the control group (p=0.005). As for the perinatal outcome, high rate of preterm deliveries was observed in the abruptio placenta group (p<0.001). Newborn in the abruptio placenta group had higher rate of NICU admission (p<0.001), Apgar score less than 7 in 5 minute (p<0.001) and stillbirth (p<0.001) as compared to the control group. There were four cases of early neonatal death in the abruptio placenta group in this study p=0.176.

Conclusion:

This study showed that pre-eclampsia, PPROM and history of abdominal massage are significant risk factors of abruptio placenta. There was statistically significant difference in the maternal complications (PPH, DIVC, blood transfusion and ICU admission) and perinatal outcome (prematurity, Apgar score less than 7 in 5 minute, NICU admission and stillbirth).

Keywords: *Abruptio placenta, incidence, risk factors, maternal outcomes, neonatal outcomes*

Introduction

Placental abruption (also referred to as abruptio placentae) is defined as partial or complete detachment of placenta prior to the delivery of fetus. It is a significant cause of both maternal morbidity and neonatal morbidity and mortality, particularly when it occurs preterm. Abruptio placentae complicates approximately 2 to 10 per 1000 births[1]. In one large series of over 500 abruptions with a live birth, 60.4 percent occurred at term, 25.3 percent occurred at 32 to 36 weeks, and 14.3 percent occurred before 32 weeks[2].

Despite extensive research, the majority of cases of abruptio placentae continue to be of unknown etiology. However, there are several identified risk factors which include high parity, advanced maternal age, low socioeconomic status, cigarette smoking, abdominal trauma, alcohol use, maternal hypertension, polyhydramnios, multiple pregnancies, thrombophilia and prior history of abruption[3-5].

For the mother, the potential consequences of abruptio placenta are primarily related to the severity of the placenta separation, meanwhile the risks to the fetus are related to both the severity of the separation and the gestational age at which the delivery occurs. There may be no significant complications with mild placental separation. However, as the degree of the placental separation increases, the maternal and neonatal adverse outcome also increase[6].

Good maternal outcome is dependent on the holistic management of hemodynamic status. As compared to pregnancies without placenta abruption, the perinatal mortality with abruptio

placenta is approximately 20-fold higher[7]. Because of the possible detrimental feto-maternal effect of abruptio placenta, we conducted this study to evaluate its prevalence and associated factors. Clinicians may provide extra caution in managing patients in the presence of these factors.

Material and Methods

This case-control study was performed in Hospital Universiti Sains Malaysia (HUSM), Kelantan over a period of 13 years from January 2008 to December 2020. The study was approved by the Human Research Ethics Committee Universiti Sains Malaysia (USM/JEPeM/21040313). Samples were recruited using Simple Random Sampling Generator using Microsoft Excel Najib (2015). After performing the systemic random sampling, 150 patients at 24 weeks gestation and above were included in this study as case group, meanwhile 150 patients who delivered without abruptio placenta were selected as the control group to make the comparison. Women with placenta praevia, indeterminate antepartum hemorrhage, vasa praevia and local trauma of the genital tract were excluded from this study. The information of each patient's data such as socio-demographic data, maternal outcome and neonatal outcome were recorded using the data collection form or proforma. Patients with inadequate information were excluded.

Data was entered and analysed using the Statistical Package for the Social Sciences (SPSS) version 27.0. For the descriptive analysis, the data was presented as mean (SD) for continuous variables and n (%) for categorical variables. Data was analysed using Pearson's Chi-square test and Fisher's exact test to identify the association of maternal and perinatal outcome

between both groups. The p value less than 0.05 ($p<0.05$) was considered statistically significant. Simple Logistic Regression (SLR) tests were applied in the univariate analysis. Variables with p value less than 0.25 or clinically important in the univariate analysis were selected for the multivariate analysis. We used forward, backward, and manual methods to determine our final model. Then, we used the Multiple Logistic Regression (MLR) test to analyse the multivariate analysis. All assumptions for the tests were met. Variables comparison with a p-value less than 0.05 is considered significant.

Results

The total number of abruptio placenta cases in HUSM from 2008 until 2020 were 288. From that, only 223 cases fulfilled the inclusion and exclusion criteria. There were 69 (46.0%) of grade 1 abruptio placenta cases, followed by 70 (46.7%) grade 2 and 11 (7.3%) grade 3 cases.

The sociodemographic characteristics of the study population as shown in Table 1. The results of the data showed that mean age was 30.0±6.0 years old with patient's age predominantly 30-34 years old in both groups. The majority of the patients were Malay (95.0%) and primigravida (59.0%) in both groups. Most of the patients' BMI were in the normal weight category in both groups.

Majority of patients in our study presented with abdominal pain with per vaginal bleeding (53.3%), followed by abdominal pain without per vaginal bleeding (28.0%) and abdominal

pain with blood-stained leaking liquor in 16.0% of cases. Only four (2.7%) patients presented with reduced fetal movement.

From the recruited women, we observed the risk factors and antenatal problems throughout their pregnancy. Based on Table 2, we found that majority of the patients in the abruptio placenta group had hypertension (62.0%). Out of this, most of the patients were in the pre-eclampsia group (45.1%) and gestational hypertension (33.3%). There were only 17 (18.2%) cases of chronic hypertension and three (3.2%) cases of eclampsia. Patients with pre-eclampsia and gestational hypertension were found to have significantly higher risk to develop abruptio placenta with p-value of <0.001 and 0.006 respectively. On the contrary, the numbers of patients in non-abruptio placenta group having chronic hypertension are statistically higher than the abruptio placenta cases (p=0.006). Other identifiable risk factors of abruptio placenta in this study were PPROM (p<0.001) and abdominal massage (p=0.032). There were six (4.0%) abruptio placenta cases had polyhydramnios and two (1.3%) had history of trauma and they were not statistically significant (p=0.520 vs p=0.156, respectively).

In Table 3, univariate analysis showed that there was a significant association between gestational hypertension (Crude OR 2.531, 95% CI 1.285-4.982, p=0.007), pre-eclampsia (Crude OR 4.098, 95% CI 2.095-8.019, p<0.001), PPROM (Crude OR 5.252, 95% CI 1.940-14.220, p=0.001), history of abdominal massage (Crude OR 7.294, 95% CI 0.886-60.029, p=0.065) and abruptio placenta compared to the non-abruptio placenta group. In the multivariate analysis, the final model only consisted of pre-eclampsia, PPROM and history of abdominal massage, in which pre-eclampsia carried odds of 4.656 (adj OR 4.656, 95% CI 2.214-9.789, p<0.001) in developing abruptio placenta when PPROM and history of abdominal

massage were controlled. Meanwhile, patients with PPROM had odds of 5.377 compared to those without PPROM (Adj OR 1.854, 95% CI 1.854-15.596, p=0.002) when adjusting for pre-eclampsia and history of abdominal massage. History of abdominal massage has a significant association with abruptio placenta with odds of 10.491 (Adj OR 10.491, 95% CI 1.188-92.636, p=0.034).

We observed the comparison of maternal outcomes of mothers with abruptio placenta versus non-abruptio placenta cases. The distribution of maternal outcomes in study population are presented in Table 4. Most of the patients with abruptio placenta delivered via LSCS (66.7%). On the contrary, majority of patients in the non-abruptio placenta group delivered via SVD (60.0%). There was a significant association between the mode of delivery in both groups (p< 0.001).

The commonest maternal complications in the abruptio placenta group were postpartum haemorrhage (PPH) (54.0%) and blood transfusion (36.0%). 13 patients had severe PPH with estimated blood loss of more than 2000mls as compared to only one case in the non-abruptio group (p<0.001). Other maternal complications include Couvelaire uterus (9.3%), disseminated intravascular coagulopathy (DIVC) (6.7%), acute renal failure (2.7%), ICU admission (10.7%) and hysterectomy (10.7%). All of the above complications were statistically significant except for acute renal failure (p=0.176) and hysterectomy (p=0.652). There was no maternal mortality case in our study.

We also made comparison of maternal complications between mode of delivery (vaginal versus caesarean section) in abruptio placenta cases. Our study found that those delivered via caesarean section developed more severe complications as compared to those delivered via vaginal delivery. There were 13 (13.0%) of cases with severe PPH with estimated blood loss of more than 2000mls and all of them delivered via caesarean section (p=0.011). Other significant maternal complications in this table included DIVC (p=0.021), Couvelaire uterus (p=0.005) and ICU admission (p=0.003).

Comparison of perinatal outcomes between case and control group was presented in Table 5. Most of the neonates in the abruptio placenta group were born preterm (71.3%) as compared to the non-abruptio placenta group whereby only 42 (28.0%) were born preterm making it statistically significant (p<0.001). There were significant association between all the perinatal outcomes upon comparing both groups such as Apgar score less than 7 in 5 minutes, NICU admission and stillbirth (p<0.001) except for early neonatal death (p=0.176).

Discussion

The separation of the placenta from its implantation site in the uterus prior to delivery of the fetus or known as abruptio placenta or placental abruption has small incidence, ranging from 0.2 to 0.7%. The incidence in our study was 288 cases in 103,042 of deliveries (0.3%) which was comparable to other studies done in Malaysia, Thailand and Netherlands[8-11]. Despite the small incidence, it carries a devastating maternal and neonatal morbidity. A variety of risk factors were associated with abruptio placenta including increasing maternal age, high parity, hypertensive disorder in pregnancy, multiple pregnancy and polyhydramnions. The

associations between these conditions and risk of abruptio placenta were not consistent in previous studies.

This study is a retrospective case-control study to evaluate the risk factors as well as maternal and fetal outcomes of abruptio placenta. From the socio-demographic data, the number of abruptio placenta cases were highest in the age group 30-34 years old (29.3%) as the largest portion of our patients were in this age group (32.3%). This contradicts from a previous study in HUSM in 1997 whereby most of the abruptio placenta cases were in the 35-39 years old (48.8%)[9]. These findings however are consistent with a study carried out by Mishra R et al in India in 2019 whereby 40.0% of abruptio placenta cases were in the 30-35 years of age[10]. There were 69 (46.0%) of grade 1 abruptio placenta cases, followed by 70 (46.7%) grade 2 and 11 (7.3%) grade 3 cases in our study which correlate with a study done in Finland in 2010[12].

Most of the patients with abruptio placenta in this study were primigravida (60.0%), followed by multipara (25.3%) and grandmultipara (14.7%). This correlates with a study done in Thailand in which 52.4% were primigravida (n=54)[13]. This finding contradicts a study done by Zanariah in HUSM in 1997 in which 116 (57.7% of) the patients were in the grandmultiparity group and another study by Abirami et al in 2020 that demonstrated the incidence of abruptio placenta increased with parity more than four[9,14]. However, our study found that patients with parity more than 5 had a three-fold increase as compared with the primigravida and multipara in developing abruptio placenta (14.7% of grandmultipara in abruptio placenta group versus 5.3% in non-abruptio placenta cases). In the state of Kelantan where HUSM is located, the

predominant race is Malay. Hence, this correlates with the racial distribution in this study in which 94.7% of the cases were Malay.

In our study, the commonest symptoms of abruptio placenta were abdominal pain with per vaginal bleeding (53.3%), followed by abdominal pain without per vaginal bleeding (28.0%) and blood-stained leaking liquor (16.0%). Only four patients presented with reduced fetal movement (2.7%) in which all of them had macerated stillbirth (MSB). This is consistent with previous study in HUSM that showed most of the patients presented with abdominal pain with PV bleeding (n=139, 69.2%) and another study in China that demonstrated 42 (68.0%) of cases presented with abdominal pain[9,15].

In relation to the associated risk factors, our study found that most of the patients with abruptio placenta had hypertension 93 (62.0%). Out of this, 42 (45.1%) patients had pre-eclampsia, 31 (33.3%) patients had gestational hypertension and 17(18.3%) were in chronic hypertension group. This correlates to another study which found the commonest risk factor for abruptio placenta was hypertension[9,13,16]. Other identifiable risk factors of abruptio placenta in this study were previous history of abruptio placenta ($p=0.004$), PPROM ($p<0.001$) and abdominal massage ($p=0.032$). There were six (4.0%) abruptio placenta cases had polyhydramnios and two (1.3%) had history of trauma. This finding corresponds to a study done in HUSM in 1997 whereby 51 (25.4%) cases had abdominal massage, which was a cultural belief and tradition more frequently practised more than 20 years ago[9].

Univariate analysis in our study showed that there was a significant association between age, chronic hypertension, gestational hypertension, pre-eclampsia, PPROM, history of abdominal massage and abruptio placenta compared to the non-abruptio placenta group. In the multivariate analysis, the final model only consisted of pre-eclampsia, PPROM and history of abdominal massage, in which all of them carried higher risk of developing abruptio placenta with adjusted odds of 4.656, 1.854 and 10.491, respectively.

In our study, majority of the abruptio placenta cases delivered via LSCS (66.7%) in which most of the indications were for fetal compromise (57.0%), whereby in the control group, most of the patients delivered via SVD (60.0%). Other indications of emergency caesarean section in our study include worsening maternal condition due to vaginal bleeding (17.0%), unfavourable cervix (11.0%) and poor progress (5.0%). There were 50 (30.0%) of cases in abruptio placenta who delivered vaginally via SVD, instrumental delivery and assisted breech delivery. Most of these patients were in the grade 1 abruptio placenta group with favourable cervix, hence they were given a trial of labour by amniotomy and pitocin augmentation. 16 (32.0%) of them presented with imminent delivery and delivered within 15 to 20 minutes upon arrival to our labour room. 16 (32.0%) of the patients delivered vaginally had stillbirth during diagnosis of abruptio placenta and were haemodynamically stable, hence they were allowed for vaginal delivery. These results were consistent with a study conducted in Thailand in which 87 (84.5%) delivered via LSCS while 16 (15.5%) delivered vaginally and Taiwan whereby 173 (52.1%) underwent caesarean section [13,17].

The maternal complications in relation to abruptio placenta in our study includes PPH (54.0%), DIVC (6.7%) and Couvelaire uterus (9.3%). Majority of the PPH were attributed to uterine atony. Upon comparing the complications between patients who delivered via LSCS and vaginally, our study found that those delivered via LSCS had more severe complications. There were 13 (8.7%) patients complicated with severe postpartum haemorrhage in our study with estimated blood loss of more than 2000mls and all of them delivered via emergency caesarean section. Out of this, 8 developed DIVC, 9 had Couvelaire uterus and 3 underwent caesarean hysterectomy. All of them required blood transfusion with packed cells and DIVC regime (platelet, fresh frozen plasma and cryoprecipitate) while 10 of them required admission to intensive care unit (ICU). As for the patients with abruptio placenta who delivered vaginally, 32 (64%) of them had PPH in which 16 (50%) required blood transfusion. There were 45 patients delivered via LSCS complicated with PPH and out of this, 38 (84.4%) required blood transfusion. The result is also the same as a previous study conducted in HUSM which showed that 75 (37.3%) cases complicated with PPH and 69 (34.3%) had DIVC and another study in India with 49 (35.0%) cases of PPH[9,18,19]. None of the patients in our case group had maternal mortality.

Majority of the neonates in the abruptio placenta group were born prematurely (less than 37weeks of gestation) (71.3%). On the contrary, in the non-abruptio placenta group, most of the neonates were born term (72.0%). There was a significant difference in the gestational age at the time of delivery between both groups ($p<0.001$).

The neonates in the abruptio placenta cases were more likely to be born with Apgar score less than 7 in 5 minutes (47.6%)[13,20-22]. This corresponds to the results demonstrated in our study whereby there were 42 (28.0%) born with low Apgar score as compared to 13 (8.7%) in the control group. 61 (40.7%) neonates in the case group required admission to NICU while only 16 (8.7%) required NICU admission in the control group. All babies born with low Apgar score were admitted to NICU due to asphyxia, while the remaining 19 babies were admitted for prematurity and respiratory distress syndrome.

Our study showed that there were 28 cases (18.7%) of stillbirth in abruptio placenta cases and 8 cases (5.3%) in the control group. In the abruptio group, 17 of them were fresh stillbirth (FSB) in which 11 were delivered via LSCS for fetal bradycardia and 6 delivered via SVD. Five of the FSB cases were in the severe prematurity group (less than 30 weeks of gestation) and one of them was diagnosed with intrauterine death intrapartum. 16 of FSB cases were in the grade 3 abruptio placenta and only 2 patients presented with grade 2 abruptio placenta. Another study conducted in Thailand had similar results whereby there were 13 (12.6%) of stillbirth cases[13]. More cases of intrauterine death 110 (54.7%) were demonstrated by Zanariah in 1997 which was due to most of the patients were already in grade 2 and grade 3 abruptio placenta during the admission to the hospital[9]. In our study, there were four (2.7%) babies in the abruptio placenta group had early neonatal death in which all of them delivered via LSCS. 3 of them were premature babies of less than 32 weeks gestation and 1 was born at 38weeks of gestation. All passed away due to severe asphyxia with multi-organ failure.

This study was the latest study on abruptio placenta conducted in HUSM after 20 years. From this study, it is shown that abruptio placenta imposes significant maternal and perinatal complications. The limitation of this study was it is only a retrospective case-control study that involves only one centre that may not represent the real figure. Hence, further research is needed, in order to identify more risk factors contributing to abruptio placenta in Malaysia population.

Conclusion

Our study showed that pre-eclampsia, PPROM and history of abdominal massage are risk factors most significantly associated with abruptio placenta. There was statistically significant difference in the maternal complications (PPH, DIVC, blood transfusion and ICU admission) and perinatal outcome (prematurity, Apgar score less than 7 in 5 minute, NICU admission and stillbirth) upon comparing the abruptio placenta with non-abruptio placenta group.

Tables and Figures

Table 1: Socio demographic characteristics in the study population (n=300)

Variables	Overall n(%)	Abruptio placenta **(Case group)** n(%)	Non-abruptio placenta **(Control group)** n(%)
Age, years*	30.0 (6.0)	29.1 (6.3)	30.9 (5.4)
<20	10 (3.3)	8 (5.3)	2 (1.3)
20-24	50 (16.7)	34 (22.7)	16 (10.7)
25-29	76 (25.3)	33 (22.0)	43 (28.7)
30-34	97 (32.3)	44 (29.3)	53 (35.3)
35-39	44 (14.7)	21 (14.0)	23 (15.3)
≥40	23 (7.7)	10 (6.7)	13 (8.7)
Ethnic			
Malay	285 (95.0)	142 (94.7)	143 (95.3)
Chinese	11 (3.7)	6(4.0)	5 (3.3)
Siam	4 (1.3)	2(1.3)	2 (1.3)
Body mass index (kg/m^2)			
Underweight (<18.5)	11 (3.7)	5 (3.3)	6 (4.0)
Normal weight (18.5-24.9)	126 (42.0)	65 (43.3)	61 (40.7)
Overweight (25-29.9)	88 (29.3)	55 (36.7)	33 (22.0)
Obese (≥30)	75 (25.0)	25 (16.7)	50 (33.3)
Parity			
Primigravida	177 (59.0)	90 (60.0)	87 (58.0)
2-4	93 (31.0)	38 (25.3)	55 (36.7)
≥5	30 (10.0)	22 (14.7)	8 (5.3)

**mean (SD).*

Descriptive statistics applied

Table 2: Risk factors in the study population (n=300)

Risk Factors	Abruptio placenta **(Case group)** n(%)	Non-abruptio placenta **(Control group)** n(%)	P-value
Previous history of abruptio			
No	142 (94.7)	150 (100)	0.004
Yes	8 (5.3)	0 (0)	
Hypertension			
No	57 (38.0)	87 (58.0)	0.078
Yes	93 (62.0)	63 (42.0)	
Chronic hypertension			
No	133 (88.7)	115 (76.7)	0.006
Yes	17 (11.3)	35 (23.3)	
Gestational hypertension			
No	119 (79.3)	136 (90.7)	0.006
Yes	31 (20.7)	14 (9.3)	
Pre-eclampsia			
No	108 (72.0)	137 (91.3)	<0.001
Yes	42 (28.0)	13 (8.7)	
Eclampsia			
No	147 (98.0)	149 (99.3)	0.314
Yes	3 (2.0)	1 (0.7)	
GDM			
No	98 (65.3)	94 (62.7)	0.630
Yes	52 (34.7)	56 (37.2)	
Type II DM			
No	142 (94.7)	135 (90.0)	0.129
Yes	8 (5.3)	15 (10.0)	
PPROM			
No	127 (84.7)	145 (96.7)	<0.001
Yes	23 (15.3)	5 (3.3)	
Polyhydramnios			
No	144 (96.0)	146 (97.3)	0.520
Yes	6 (4.0)	4 (2.7)	
History of abdominal massage			
No	143 (95.3)	149 (99.3)	0.032
Yes	7 (4.7)	1 (0.7)	
History of trauma			
No	148 (98.7)	150 (100.0)	0.156
Yes	2 (1.3)	0 (0.0)	

Chi-square test applied

Table 3: Factors associated with abruptio placenta using Simple and Multiple Logistic Regression

Variables	Crude OR (95% CI)	P-value[a]	Adj. OR (95% CI)	P-value[b]
Age	0.950 (0.914,0.987)	0.009	0.955 (0.910,1.003)	0.064
Ethnic	0.925 (0.427,2.005)	0.844	0.283 (0.049,1.633)	0.158
Body mass index (kg/m^2)	0.978 (0.926,1.034)	0.436	1.007 (0.938,1.081)	0.840
Parity	1.178 (0.839, 1.652)	0.344	2.309 (1.037,5.141)	0.409
Previous history of abruptio	-	0.999	-	1.000
Chronic hypertension	0.420 (0.223,0.789)	0.007	0.485 (0.214,1.098)	0.083
Gestational hypertension	2.531 (1.285,4.982)	0.007	1.571 (0.710,3.476)	0.265
Pre-eclampsia	4.098 (2.095,8.019)	<0.001	4.656 (2.214,9.789)	<0.001
Eclampsia	3.041 (0.313,29.569)	0.338	3.109 (0.320,30.238)	0.328
GDM	1.123 (0.701,1.800)	0.630	1.261 (0.509,3.127)	0.616
Type II DM	1.972 (0.810,4.802)	0.135	2.646 (0.549,12.751)	0.225
PPROM	5.252 (1.940,14.220)	0.001	5.377 (1.854,15.596)	0.002
Polyhydramnios	1.521 (0.420,5.502)	0.523	0.960 (0.062,14.791)	0.977
History of abdominal massage	7.294 (0.886,60.029)	0.065	10.491 (1.199,92.636)	0.034
Trauma	-	0.999	-	1.000

[a]*Simple Logistic Regression applied*

[b]*Multiple Logistic Regression applied*
Constant = 2.700
Forward LR, Backward LR and manual methods were applied
No multicollinearity and no interaction
Hosmer Lemeshow test, p-value= 0.112
Classification table 66.7% correctly classified
The area under Receiver Operating Characteristics (ROC) curve was 72.9% (p<0.001)

Table 4: Maternal outcomes in the study population (n=300)

Maternal Outcomes	Abruptio placenta **(Case group)** n(%)	Non-abruptio placenta **(Control group)** n(%)	P-value
Mode of delivery			
LSCS	100 (66.7)	44 (29.3)	<0.001
SVD	45 (30.0)	90 (60.0)	
Instrumental delivery	3 (2.0)	13 (8.7)	
ABD	2 (1.3)	3 (2.0)	
PPH	69 (46.0)	119 (79.3)	<0.001
No	81 (54.0)	31 (20.7)	
Yes			
EBL (mls)			
500-1000	68 (45.3)	33 (22.0)	
1001-1499	19 (12.7)	6 (4.0)	
1500-2000	23 (15.3)	6 (4.0)	
>2000	13 (8.7)	1 (0.7)	
DIVC			
No	140 (93.3)	149 (99.3)	0.006
Yes	10 (6.7)	1 (0.7)	
Couvelaire uterus			
No	136 (90.7)	150 (100)	<0.001
Yes	14 (9.3)	0 (0.0)	
Acute Renal Failure			
No	146 (97.3)	149 (99.3)	0.176
Yes	4 (2.7)	1 (0.7)	
Blood Transfusion			
No	96 (64.0)	135 (90.0)	<0.001
Yes	54 (36.0)	15 (10.0)	
Hysterectomy			
No	147 (98.0)	148 (98.7)	0.652
Yes	3 (2.0)	2 (1.3)	
ICU Admission			
No	134 (89.3)	146 (97.3)	0.005
Yes	16 (10.7)	4 (2.7)	
Maternal Mortality			
No	150 (100.0)	150 (100.0)	-
Yes	-	-	

Chi-square test applied

Table 5: Fetal outcomes in the study population (n=300)

Fetal Outcomes	Abruptio placenta **(Case group)** n(%)	Non-abruptio placenta **(Control group)** n(%)	P-value
Gestational Age			
< 30 weeks	13 (8.7)	3 (1.0)	<0.001
30-34 weeks	45 (30.0)	11 (7.3)	
34-37weeks	49 (32.7)	28 (18.7)	
>37 weeks	43 (28.7)	108 (72.0)	
Apgar Score <7 In 5minutes			
No	108 (742.0)	137 (91.3)	<0.001
Yes	42 (28.0)	13 (8.7)	
NICU Admission			
No	89 (59.3)	134 (89.3)	<0.001
Yes	61 (40.7)	16 (10.7)	
Stillbirth			
No	122 (81.3)	142 (94.7)	<0.001
Yes	28 (18.7)	8 (5.3)	
FSB	17 (60.7)	2 (25.0)	<0.001
MSB	11 (39.3)	6 (75.0)	
Early Neonatal Death			
No	146 (97.3)	149 (99.3)	0.176
Yes	4 (2.7)	1 (0.7)	

Chi-square test applied

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9.0 APPENDICES

9.1 Tables

Table 1: Symptoms among abruptio placenta cases (n=150)

Symptoms	**n (%)**
Abdominal pain with per vaginal bleeding	80 (53.3)
Abdominal pain without per vaginal bleeding	42 (28.0)
Abdominal pain with blood-stained leaking liquor	24 (16.0)
Reduced fetal movement	4 (2.7)
Total	150 (100)

Table 2: Maternal outcomes upon comparing mode of delivery in abruptio placenta (n=150)

Maternal outcomes	Vaginal delivery n (%)	Caesarean section n (%)	P-value
PPH			
No	15 (30.0)	54 (54.0)	0.005
Yes	35 (70.0)	46 (46.0)	
EBL (mls)			
<500	15 (30.0)	12 (12.0)	0.011
500-1000	20 (40.0)	48 (48.0)	
1001-1499	7 (14.0)	12 (12.0)	
1500-2000	8 (16.0	15 (15.0)	
>2000	0 (0.0)	13 (13.0)	
DIVC			
No	50 (100.0)	90 (90.0)	0.021
Yes	0 (0.0)	10 (10.0)	
Couvelaire uterus			
No	50 (100.0)	86 (86.0)	0.005
Yes	0 (0.0)	14 (14.0)	
Acute Renal Failure			
No	50 (100.0)	96 (96.0)	0.152
Yes	0 (0.0)	4 (4.0)	
Blood Transfusion			
No	34 (68.0)	62 (62.0)	0.470
Yes	16 (32.0)	38 (38.0)	
Hysterectomy			
No	50 (0.0)	97 (97.0)	0.216
Yes	0 (0.0)	3 (3.0)	
ICU admission			
No	50 (100.0)	84 (84.0)	0.003
Yes	0 (0.0)	16 (16.0)	

Chi square test applied

9.2 Proforma

Patient's detail
Study ID : Age: Date of birth: Ethnicity: Date of admission: Date of discharge: Date of delivery: Gravida: Parity: Gestational age: Booking weight: Height: Latest weight: BMI: Hb pre-delivery: Smoking: Yes / No Antenatal issue: A. CHRONIC HYPERTENSION/ GESTATIONAL HYPERTENSION/ PRE ECLAMPSIA/ ECLAMPSIA B. GDM/ DM C. PREVIOUS HISTORY OF ABRUPTIO PLACENTA D. PPROM E. OTHERS _____ Presenting symptoms: …….. Scan findings: A. Singleton/ multiple pregnancy B. Lie/ presentation : …… C. Placenta : …….

D. Retroplacental clots: Yes/ No

E. AFI

Fetal heart rate/ CTG: ….bpm, normal/ suspicious/ pathological

Duration of diagnosis of abruptio placenta until delivery of baby: _____

Amount of retroplacental clots: ……..mls

PAST OBSTETRICS HISTORY

Year	**Antenatal Problem**	**MOD**	**Spontaneous/ Induction**	**Baby Weight**	**Outcome**

Maternal outcome

Mode of delivery: Spontaneous vertex delivery/ Instrumental/ Lower segment caesarean section/ hysterotomy

Estimated blood loss: ……..mls

Postpartum haemorrhage: Yes/ No. If yes, cause ……

Any additional intervention to manage PPH. Eg; Bakri balloon for uterine atony

Hemorrhagic shock: Yes/ No

Blood transfusion: Yes/ No. If yes, details of transfusion(quantity)

Packed cell:

FFP:

Platelet concentrate:

Cryoprecipitae:

Coagulation disorder/ DIVC: Yes / No

Acute renal failure: Yes/ No. If yes, any dialysis required?

Couvelaire uterus: Yes/ No

Hysterectomy: Yes/ No. Reason for hysterectomy: …….

ICU admission: Yes/ No. If yes, length of stay ….

Duration of hospital stay post op: …….

Mortality: Yes/ No. Cause of death

Perinatal outcome

Gestation at birth:

Birth weight: …….grams

Apgar score at; 1 minute of life: ……; 5 minutes of life: ……

NICU admission: Yes / No. If yes, state reason …….

Intubation: Yes/ No. If yes, state reason …….

Stillbirth
MSB: Yes / No. If yes, cause of stillbirth ……
FSB : Yes / No. If yes, cause of stillbirth ……
Early neonatal death: Yes / No. If yes, cause of death …….

9.3 Ethical Approval Letter from USM Human Research Ethical Committee

Jawatankuasa Etika
Penyelidikan Manusia USM (JEPeM)

Human Research Ethics Committee USM (HREC)

Universiti Sains Malaysia
Kampus Kesihatan
16150 Kubang Kerian, Kelantan. Malaysia.
Tel. : +609 - 767 3000/2354/2362
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12th August 2021

Dr. Nor Liyana Mohamad Sasudin
Department of Obstetrics and Gynaecology
School of Medical Sciences
Universiti Sains Malaysia
16150 Kubang Kerian, Kelantan.

JEPeM Code : USM/JEPeM/21040313
Protocol Title: A Review on Maternal and Perinatal Outcome of Abruptio Placenta in Hospital USM.

Dear Dr.,

We wish to inform you that your study protocol has been reviewed and is hereby granted approval for implementation by the Jawatankuasa Etika Penyelidikan Manusia Universiti Sains Malaysia (JEPeM-USM). Your study has been assigned study protocol code **USM/JEPeM/21040313**, which should be used for all communications to JEPeM-USM in relation to this study. This ethical approval is valid from **12th August 2021** until **11th August 2022.**

Study Site: Hospital Universiti Sains Malaysia.

The following researchers are also involved in this study:
1. Prof. Dr. Nik Mohamed Zaki Nik Mahmood
2. Dr. W. Fadhlina W. Adnan

The following documents have been approved for use in the study.
1. Research Proposal

In addition to the above mentioned document, the following technical documents were included in the review on which this approval was based:
1. Data Collection Form (Research tool)

While the study is in progress, we request you to submit to us the following documents:
1. Application for renewal of ethical approval 60 days before the expiration date of this approval through submission of **JEPeM-USM FORM 3(B) 2019: Continuing Review Application Form.**
2. Any changes in the protocol, especially those that may adversely affect the safety of the participants during the conduct of the trial including changes in personnel, must be submitted or reported using **JEPeM-USM FORM 3(A) 2019: Study Protocol Amendment Submission Form.**
3. Revisions in the informed consent form using the **JEPeM-USM FORM 3(A) 2019: Study Protocol Amendment Submission Form.**
4. Reports of adverse events including from other study sites (national, international) using the **JEPeM-USM FORM 3(G) 2019: Adverse Events Report.**
5. Notice of early termination of the study and reasons for such using **JEPeM-USM FORM 3(E) 2019.**
6. Any event which may have ethical significance.
7. Any information which is needed by the JEPeM-USM to do ongoing review.
8. Notice of time of completion of the study using **JEPeM-USM FORM 3(C) 2019: Final Report Form.**

JEPeM
JAWATANKUASA ETIKA PENYELIDIKAN MANUSIA

Please note that forms may be downloaded from the JEPeM-USM website: **www.jepem.kk.usm.my**

JEPeM-USM is in compliance with the Declaration of Helsinki, International Conference on Harmonization (ICH) Guidelines, Good Clinical Practice (GCP) Standards, Council for International Organizations of Medical Sciences (CIOMS) Guidelines, World Health Organization (WHO) Standards and Operational Guidance for Ethics Review of Health-Related Research and Surveying and Evaluating Ethical Review Practices, EC/IRB Standard Operating Procedures (SOPs), and Local Regulations and Standards in Ethical Review.

Thank you.

"PRIHATIN RAKYAT: DARURAT MEMERANGI COVID-19"

"WAWASAN KEMAKMURAN BERSAMA 2030"

"BERKHIDMAT UNTUK NEGARA"

Sincerely,

ASSOC. PROF. DR. AZLAN HUSIN
Chairperson
Jawatankuasa Etika Penyelidikan (Manusia) JEPeM
Universiti Sains Malaysia