

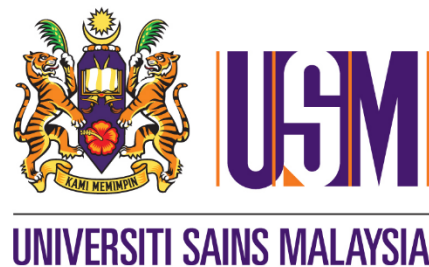
**PREVALENCE AND RISK FACTORS OF
PRETERM BIRTH IN HUSM
CASE – CONTROL STUDY
FROM JANUARY 2014 – DECEMBER 2015**

BY

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TABLE OF CONTENTS

ACKNOWLEDGEMENTS	i
LIST OF TABLE	vii
LIST OF FIGURES	ix
LIST OF ABBREVIATIONS	x
ABSTRACTS	xiii
ABSTRAK (BAHASA MELAYU)	xiv
ABSTRACT (ENGLISH VERSION)	xvii
CHAPTER	xix
1.0 KELANTAN AND MATERNAL HEALTH CARE	xx
1.1 Introduction To The State Of Kelantan	xx
1.2 Maternal Health Care in Kelantan	xxii
2.0 THE SCHOOL OF MEDICAL SCIENCES	xxiv
2.1 Universiti Sains Malaysia	xxiv
2.2 The Department Of Obstetrics And Gynecology	xxvii

INTRODUCTION	1
3.0 INTRODUCTION OF STUDY	2
LITERATURE REVIEW	4
4.0 LITERATURE REVIEW	5
4.1 Incidence and Prevalence of Preterm Birth.....	5
4.2 Risk Factor For Preterm Birth	7
4.3 Subtype Of Preterm Birth	7
4.4 Justification And Rationale of the Study	9
OBJECTIVES.....	10
5.0 OBJECTIVES	11
5.1 General Objective.....	11
5.2 Specific Objectives:	11
METHODOLOGY.....	12
6.0 METHODOLOGY	13
6.1 Materials And Methods	13
6.2 Study Participants.....	17
6.3 Sample Size Determination	18

6.4 Sampling Method	25
6.5 Validity and Reliability of the Measurement Tool	26
6.6 Ethical Approval	27
6.7 Flow Chart of The Study	28
RESULTS	29
7.0 RESULT	30
7.1 Results of Prevalence	30
7.2 Descriptive Analysis	33
7.3 Univariable Analysis	41
7.4 Multivariable Analysis	50
7.4.1 Checking Interaction and Multicollinearity	53
7.4.2 Checking Assumptions	53
DISCUSSION	60
8.0 DISCUSSION	61
CONCLUSION	66
9.0 CONCLUSION	67

LIMITATIONS	68
10.0 LIMITATION OF STUDY	69
RECOMMENDATION	70
11.0 RECOMMENDATION	71
REFERENCES	72
12.0 REFERENCES	73
APPENDICES	78
13.0 APPENDICES	79
13.1 Appendix 1 (Data Collection Form)	79
13.2 Appendix 2 (Ethical Approval)	84

LIST OF TABLE

No.	Table	Content	Page
1	2.2.1	Clinic Activity In O&G Clinic HUSM	xxix
2	2.2.2	The Number Of Outpatient Seen From 2011 To 2015 In O&G Clinic HUSM	xxx
3	2.2.3	Basic Statistic Of Delivery Of O&G, HUSM From 2011 To 2015	xxxii
4	6.3.1	Sample Size According To Risk Factor According To Socio-Demographic And Behavior	20
5	6.3.2	Sample Size According To Risk Factors Associated With Previous Pregnancy And Reproductive Characteristic	21
6	6.3.3	Sample Size According To Risk Factors Associated With Current Pregnancy Characteristics	22
7	6.3.4	Sample Size According To Clinical Subtype	23
8	6.3.5	Sample Size According To Gestational Age At Delivery	24
9	7.1.1	Distribution Of Preterm Birth And Term Birth According To Gestational Age	31
10	7.1.2	Distribution Of Preterm Birth And Term Birth According To Clinical Subtype/Causes	32
11	7.2.1	Numbers And Rate Of Risk Factor According To Maternal Socio-Demography	33

12	7.2.2	Number And Rate Risk Factor According To Previous Pregnancy And Reproductive Characteristic	36
13	7.2.3	Number And Rate Of Risk Factor According To Current Pregnancy And Prenatal Outcome	38
14	7.3.1	Univariable Analysis Of Preterm Birth According To Maternal Socio-Demography Status	42
15	7.3.2	Univariable Analysis Of Previous Pregnancy And Reproductive Characteristic	44
16	7.3.3	Univariable Analysis Of Current Pregnancy And Prenatal Outcome	46
17	7.4.1	Associated Risk Factors Of Preterm By Multiple Logistic Regression	51
18	7.4.2.1	Hosmer- Lemeshow Test	54
19	7.4.2.2	Classification Table	54
20	7.4.2.3	Area Under The Curve	56
21	7.4.2.4	Associate Risk Factors Of Preterm Birth In HUSM 2014-2015	58

LIST OF FIGURES

No.	Figures	Content	Page
1	7.4	Area Under The ROC Curve	55

LIST OF ABBREVIATIONS

ACOG	American College of Obstetricians and Gynecologists
BMI	Body Mass Index
CI	Confident Interval
CCU	Cardiac Care Unit
Df	Degree of Freedom
DM	Diabetes Mellitus
DR	Doctor
gm	Gram
HRPZ 2	Hospital Raja Perempuan Zainab II
HUSM	Hospital Universiti Sains Malaysia
ICD	International Classification of Diseases
ICU	Intensive Care Unit
IUGR	Intrauterine Growth Restriction
Kg	Kilogram
LMP	Last Menstrual Period
m ²	Meter Square

MIPTB	Medically Indicated Preterm
MMR	Maternal Mortality Rate
n	Number of Sample Size
NICU	Neonatal Intensive Care Unit
OR	Odd Ratio
PROM	Premature Rupture of Membranes/ Pre-Labor Rupture Of Membranes
Prof	Professor
PPROM	Preterm Prelabour Rupture of Membrane
PTB	Preterm Birth
ROC	Receiver Operating Characteristic
RCOG	Royal College of Obstetrician and Gynaecologist
SLR	Simple Logistic Regression
SMS	School of Medical Sciences
SPSS	Statistical Package for the Social Sciences
SVD	Spontaneous Vertex Delivery
USMK	Universiti Sains Malaysia Kelantan

WHO

World Health Organization

ABSTRACTS

ABSTRAK (BAHASA MELAYU)

Tajuk

Prevalens dan faktor risiko kelahiran pramatang di HUSM

Kes Retrospektif - kajian kawalan dari Januari 2014 - Disember 2015

Objektif

Kajian ini dijalankan untuk mencari prevalens kelahiran pramatang dan untuk mencari faktor risiko untuk kelahiran pramatang di HUSM pada tahun 2014 hingga 2015. Kajian ini juga, melibatkan pembahagian kelahiran pramatang mengikut sebab kelahiran dan mengikut usia kandungan semasa kelahiran.

Kajian ini juga bertujuan bagi membandingkan faktor risiko kelahiran pramatang mengikut sosio – demografi ibu, sejarah kelahiran terdahulu dan status kandungan dan prenatal ibu pada masa kajian. Selain itu, kajian ini juga menentukan kaitan diantara faktor risiko dengan kelahiran pramatang.

Metodologi

Kajian kes kawalan retrospektif telah dijalankan di HUSM untuk tempoh dari 2014 hingga 2015. Kajian ini melibatkan 418 kelahiran pramatang dan 418 kelahiran cukup bulan di HUSM. Semua rekod perubatan mereka telah dikaji semula dan maklumat berkaitan telah dimasukkan ke dalam borang pengumpulan data standard. Chi -square digunakan bagi tujuan perbandingan taburan pembolehubah antara kumpulan. Analisis univariat juga digunakan bagi menilai kaitan antara pembolehubah bebas dan kelahiran pramatang. analisis multivariat akan digunakan dan semua pembolehubah menunjukkan hubungan yang signifikan dengan kelahiran pramatang dalam analisis univariat akan digunakan untuk mengira nisbah ganjil (OR) potensi faktor risiko berkaitan dengan kelahiran pramatang.

Keputusan

Terdapat 418 kelahiran pramatang dan 418 kes kelahiran cukup bulan yang terlibat dalam kajian ini. Prevalens kelahiran pramatang adalah 6.8%. Majoriti pesakit adalah berbangsa Melayu (98.1%). Kelahiran pramatang spontan (SPTB) adalah 52.2%, kelahiran pramatang disebabkan pecah air mentuban (PPROM) adalah 31.6% dan kelahiran pramatang disebabkan masalah perubatan (MIPTB) adalah 16.3%. Berdasarkan usia kandungan, kelahiran semasa usia kandungan 32 minggu hingga <37 minggu berlaku paling tinggi iaitu 90.2%, diikuti oleh pramatang sederhana (28 minggu - 32 minggu) 8.1% dan paling pramatang (kurang daripada 28 minggu) 1.7%. Multipara adalah lebih rendah peluang untuk mempunyai kelahiran pramatang sebanyak 39% berbanding pesakit nulliparous dan granmultipara. Pesakit yang mempunyai sejarah kelahiran pramatang akan meningkatkan

risiko pramatang sebanyak 10.83 nisbah ganjil berbanding dengan mereka yang tidak mempunyai sejarah kelahiran pramatang (CI: 0.62-25.40, p-value <0.001). Sementara itu, pesakit dengan tekanan darah tinggi dan DM mempunyai 2.75 dan 2.00 nisbah ganjil kemungkinan kelahiran pramatang berbanding dengan mereka yang tidak mempunyai tekanan darah tinggi dan DM sebagai comorbid (CI:1.56-4.86, p-value <0.001) (CI:1.27-3.18, p-value=0.003). Pesakit yang bekerja meningkatkan kemungkinan mendapat kelahiran pramatang sebanyak 3.40 nisbah ganjil jika dibandingkan dengan surirumah (CI:2.40-4.82, p-value <0.001). Akhir sekali, pesakit yang melahirkan bayi lelaki mempunyai 70% kemungkinan pendedahan kepada kelahiran pramatang berbanding pesakit dengan bayi perempuan (CI:1.24-2.29, p-value=0.001).

Kesimpulan

Pengesanan awal dan rawatan penyakit di kalangan pesakit berisiko terutama yang mempunyai masalah tekanan darah tinggi dan kencing manis, pencegahan awal kepada pesakit yang mempunyai sejarah kelahiran pramatang akan dapat mengurangkan kadar kelahiran pramatang.

ABSTRACT (ENGLISH VERSION)

Topic

Prevalence and Risks Factor of Preterm Birth in HUSM

Retrospective Case - control study from January 2014 – December 2015

Objective

This study was designed to identify the prevalence and risk factors for preterm birth in HUSM in year 2014 to 2015

This study looked into the risk factors of preterm birth according to maternal socio – demographic, previous pregnancy and reproductive characteristics, and current maternal and prenatal pregnancy status.

Methodology

This retrospective case control study was conducted in HUSM for period from 2014 to 2015. The study included 418 preterm birth and 418 term birth who delivered in HUSM. All their medical record were reviewed and related information were entered in a standard data collection form. Chi –square is use to compare distribution of variables between groups. Univariable analysis used to evaluate association between independent variables and preterm birth. Multivariable analysis will be use and all the variable displaying significant relationship with preterm birth in the univariable analysis will be employed to calculate odd ratio (OR) of potential risk factor associate with preterm birth.

Results

There were 418 preterm birth and 418 term birth cases involved in this study. The prevalence of preterm birth was 6.8%. The majority of patient was Malay which is 98.1% and the rest was Chinese (1.9%). Spontaneous preterm birth (SPTB) give raised to 52.2% of the delivery, preterm pre-labour rupture of membrane (PPROM) was 31.6% and medically indicated preterm birth (MIPTB) birth was 16.3%. Base on gestational age, mild preterm (32 weeks till < 37 weeks) occur the most 90.2%, followed by late preterm (28 weeks – 32 weeks) 8.1% and extremely preterm (less than 28 weeks) 1.7%. Multipara patient was lower the chance to have preterm labor by 39% compared to patient with nulliparous. Patients that had previous preterm birth increased the risk of preterm by 10.83 compared to those who had no history of preterm birth before (CI: 0.62-25.40, p-value <0.001). Meanwhile, patient with hypertension and DM had 2.75 odds and 2.00 odds of preterm birth compared to those who had no Hypertension and DM as comorbid (CI:1.56-4.86, p-value <0.001) (CI:1.27-3.18, p-value=0.003). Working patient increased the odds of getting preterm birth by 3.40 when comparing to not working patient (CI:2.40-4.82, p-value <0.001). Lastly, patient with baby boy had 70% odds of exposing to preterm birth compared to patient with baby girl (CI:1.24-2.29, p-value=0.001).

Conclusion

Early detection and treatment of disease or disorder among pregnant patient especially hypertension, diabetes, and started preventive measure for those with previous history of preterm birth can improve the outcome for preterm birth and will reduce the preterm prevalence rate.

CHAPTER

1.0 KELANTAN AND MATERNAL HEALTH CARE

1.1 Introduction To The State Of Kelantan

Kelantan is situated in the northeast part of peninsular Malaysia and facing the South China Sea. Roughly, it has a total area of 14,900 square kilometers. It share the bonders with Pahang, Perak, and Terengganu and on the north is the Thailand.

Based on the latest population census, Kelantan has a population of 1.7 million. Kelantan has a GDP per capita in 2006 at RM7, 985, which is about a fraction that of other richer states like Selangor and Penang. Kelantan has become the first state to introduce the gold dinar and silver dirham as official currency.

Most of the Kelantan population are ethnic Malay, and under the Malaysian constitution, all Malays are Muslims. Islam is the most influential religion in the state. Kelantan has a chiefly agrarian economy dominated by rice, rubber and tobacco. Fishing along its 96-kilometer coastline is also an important economic activity. Cottage industries which employ traditional skills in handicraft production such as batik, woodcarving and Songket weaving are also evident. Logging activities are active given the vast remaining area of forest. In recent years, tourism, especially to offshore islands, has increased in importance. A few reputable hotels have been established and more modern shopping malls have been opened to cater for urban folks.

Kota Bharu, the capital, is the major urban Centre, and there are also plans to open up the southern portion of the state under an ambitious multimillion-dollar development project. The main market at the city centre is a top attraction.

1.2 Maternal Health Care in Kelantan

1930 was the beginning of maternal healthcare in the state of Kelantan with the building of their first general Hospital. Midwifery training was initiated then with its upgrading in 1946.

Ten years later, the national rural health Development started extensive development of health infrastructure facilities program and the state's medical and health services have improved tremendously with opening of districts hospital and health centers along with substantial social, educational and economic improvement. The medical and health services for the state are provided by nine hospital; 2 in Kota Bharu districts and one in each except for district Bachok and Jeli.

There are also 55 government health clinics (Klinik kesihatan) and 230 government health clinic (Klinik Desa). Out of nine hospital, there are 4 government hospital with specialist in Kelantan, namely Hospital Raja Perempuan Zainab 11 (HRPZ11), Hospital University Sains Malaysia (HUSM), Hospital Kuala Krai and Hospital Tanah Merah.

Improvement of medical and health services in the state is clearly reflected by increasing in numbers of hospital deliveries, reduction in perinatal mortality and maternal mortality. The maternal rate (MMR) in Kelantan has declined in 1980 from 1.1 per 1000 live birth to 0.55 per 1000 live birth in 1995.

After that year, the cases of maternal death climbing up back then started 2009 the cases reducing back to 20 cases in 2009, 18 cases in 2010 and 9 cases in 2011.

2.0 THE SCHOOL OF MEDICAL SCIENCES

2.1 Universiti Sains Malaysia

Universiti Sains Malaysia (USM), the third University in Malaysia was established in 1969 in Penang. Subsequently, in 1983 to 1985 it set up two branch campuses, the first in Kelantan followed by the second in Perak. USM Perak branch houses the various schools of engineering while USM Kelantan branch; initially has its School of Medical Sciences (SMS) and Hospital Universiti Sains Malaysia (HUSM) which act as a teaching hospital and currently has another 2 campus, school of Dental Sciences and School of Health Sciences.

The uniqueness of this medical school lies in fact that it is the first medical school in the country to adopt an innovative, community oriented curriculum for its medical students. From the beginning and true to its name, USM is given the mandate to provide, promote and develop higher education in the fields of natural Sciences, Applied Sciences, Pharmaceutical Sciences, Building Sciences and Technology, Social science, Humanities and Education, with the emphasis on research and advancement of knowledge dissemination in those fields.

This campus started to develop in 1983 when the Ministry of health Malaysia handed over a newly completed hospital building to USM to act as a teaching hospital for its medical undergraduates. Then the campus only accommodated the 4th and 5th year students, and academic staff from clinical disciplines. Medical student for years 1, 2 and

3 remained at the main campus in Penang together with their lecturers and the administrative machinery of the school.

In June 1990, the whole School of Medical Sciences moved from main campus to the subcampus. This move marked the beginning of the administrative machinery of University Sains Malaysia Kelantan (USMK).

USMK is situated on 72.84 hectares of flatland in the suburbs of Kota Bharu has the potential to expand and develop. The presence of USMK in Kubang Kerian has activated commercial and housing industries. This once quiet suburbs of Kota Bharu is planned to be the satellite town in the near future.

To people in the street, HUSM is better known than any other component of this campus. This may be due to the fact that the hospital building was the first landmark of the campus or because of its direct involvement with the community. HUSM is headed by a director and assisted by two deputy directors. The various heads of department and heads of units also assist him.

The hospital opened its doors to patients in October 1983. It provides medical services like any other hospitals in the country. It also acts as a teaching hospital for the medical,

dental, and health sciences undergraduate students. With the presence of specialists and consultants in the various fields of medicine and related disciplines, it is able to be the referral center for the east coast states of peninsular Malaysia.

Services can be categorized into two, namely the outpatient service and the in patient service. Outpatient service consists of community medicine clinic that is open on all working days from 0830 – 1630, the specialist clinics that open from Sunday to Thursday and see cases by referral and appointments. The third outpatient clinic is accident and emergency unit that is open round the clock to attend to all kind of urgent case.

In patient service provides treatment in one of the 28 wards of HUSM. The wards are divided into various disciplines like Obstetrics and Gynecology, Surgery, Orthopedic, Psychiatry Ophthalmology, Otorhinolaryngology, Pediatric, Medical, Oncology, ICU, CCU and NICU.

As teaching hospital and referral center, HUSM undertakes to provide the best, in patient service. Specialists who are also lectures of SMS act as consultants to all cases in HUSM.

2.2 The Department Of Obstetrics And Gynecology

Up to date, the department of Obstetrics and Gynecology was staffed by 13 consultants/ specialists, 8 registrars (final year masters students), eighteen medical officers/ trainee lecturers and twelve house officers. The postgraduate program was started in 1991 and the first master of medicine candidates graduated in June 1995.

Since 1995, the department of Obstetrics and Gynecology occupied the first and second floors of the main hospital building. There were two gynecology wards on the second floor with 56 beds and two obstetrics wards on the first floor with 72 beds.

The department had a major transfer in June 1997 to new block. The new block now has a labor room, the antenatal ward and the postnatal ward. The labor room (2 Berlian) is currently on the first floor of the block. It consists of 7 labor suites, 1 admission room, 1 bed for high dependency room (HDU), 2 bed for pre eclampsia patients, 2 bed premature labor room, 1 operating theatre and 2 ultrasound room.

Adjacent to the labor room is neonatal resuscitation room with a resuscitation trolley, warmer and incubators. There is an operation theatre situated within the labor room, which is opened during office hours for emergency obstetrics procedures such as caesarean section, manual removal of placenta and also for elective case for caesarean section.

There is one registrar and 2 medical officers posted in labor room during office hours. After office hours the on call team takes charge of running the labor room. The antenatal ward (2 Baiduri and 2Akik) is situated on the second floor and has 20 beds each and the postnatal ward (2 Topaz) has 40 beds. The gynecology ward were shifted to the first floor of the old hospital block and have total 30 beds.

The obstetrics and gynecology clinic is situated on the ground floor of the same building of labor room and is equipped with 4 functioning ultrasound machines, 2 cardiotochography (CTG) machine and colposcope. The clinic runs as follow in table below.

The doctors are scheduled equally into four team A, B, C, and D to these clinics as well as the wards and duties normal working days as well as on call days.

Table 2.2.1 : Clinic Activity in Obstetrics and Gynecology HUSM

DAY	MORNING	AFTERNOON
Sunday	Antenatal outpatients clinic	Gynaecology outpatient clinic
Monday	Menopause clinic	Molar clinic, Early pregnancy assessment unit (EPAU) clinic, colposcopy clinic
Tuesday	Antenatal outpatient clinic	Gynecology outpatient clinic
Wednesday	Fertility augmentation clinic, Urogyne clinic	Postnatal clinic
Thursday	Booking antenatal clinic	Department presentation

Table 2.2.2: The Number Of Outpatient Cases Seen From 2011 To 2015 In Obstetrics And Gynecology Clinic

YEAR	Total
2011	13328
2012	14582
2013	13764
2014	12865
2015	13629

**Table 2.2.3: Basic statistic of Obstetrics and Gynecology, Hospital Universiti Sains
Malaysia from 2011 to 2015**

YEAR	2011	2012	2013	2014	2015
TOTAL DELIVERIES	6472	7295	7452	8745	9253
MODE OF DELIVERIES					
SVD	4984	5481	5810	6797	7127
Vacuum	167	160	110	146	239
Forcep	48	41	53	139	156
Caesarean Section	1356	1545	1399	1583	1659
Breech	57	68	80	80	72
Twin	73	102	88	83	82
Still Birth	62	70	71	77	73
Maternal Mortality	6	2	6	1	8

INTRODUCTION

3.0 INTRODUCTION OF STUDY

Preterm birth (PTB) is defined as birth of an infant prior to 37 weeks or 259 days from the first day of last menstrual period by the World Health Organization (Berkowitz, et al., 1998). This preterm birth can further sub-divided on the basis of gestational age: extremely preterm birth (< 28 weeks), very preterm (28 weeks to < 32 weeks), and moderate or late preterm (32 weeks to <37 weeks). These subdivisions are important as decreasing gestational age is associated with increasing neonatal mortality, disability, prolong stay in intensive care units and hence lead to increase the economic cost as overall.

The rate of preterm birth have been reported to range between 5 to 7% of live births in developed countries, but are estimated to be higher in developing countries (Beck, et al., 2010). Out of all early neonatal death, defined as deaths within the first 7 days of life that are not related to congenital malformation, 24% are because of PTB (Beck, et al., 2010). Approximately 85% of preterm births take place in Africa and Asia. In Malaysia, 50 % of neonatal deaths are because of PTB (Sim & Hong, 2008), and prevalence of preterm birth in Malaysia in year 1998 was around 10% (Zaini, et al., 2008). Besides neonatal deaths, prematurity is the major determinant of neonatal mortality and morbidity in infants.

Pathophysiology leading to PTB are still not completely understood although the aetiology is believed to be multifactorial and involves a complex interaction between fetal, placental, uterine and maternal factors (Ananth and Vintzileos, 2006). Risk factors associated with PTB include underlying socio-economic factors, behaviors, medical condition of the mother and fetus, genetic influences, environmental exposure, infertility treatment and iatrogenic prematurity (Ip et al, 2010; R et al, 2014).

Regardless of many studies done on PTB, its exact cause is yet to be identified. Therefore, preventive measures could not be successfully implemented.

About 45-50% of PTB are idiopathic or spontaneous, 30% are related to preterm prelabour rupture of membrane (PPROM) and another 15-20% is attributed by medically indicated preterm deliveries (MIPTB) for example diabetes, hypertension, pre-eclampsia and systemic lupus erythematosus (Beck, et al., 2010). Thus, proper categorization and estimation of PTB are essential for accurate determination of worldwide prevalence or incidence of PTB and for generate campaign and intervention to reduce the risk of preterm labour and delivery.

LITERATURE REVIEW

4.0 LITERATURE REVIEW

4.1 Incidence and Prevalence of Preterm Birth

Study done by Chythra R. Rao et al., (2014), a case-control study was aimed to identify the risk factors of PTB in a secondary care hospital in Southern India (Chythra R. Rao, et al., 2014). According to the World Health Organization (2012), the prevalence of preterm birth was 5.8%, which is much lower than Malaysia's prevalence (12.3%). The common risk factor associated with PTB were hypertensive disorders of pregnancy (21.4%), maternal height < 150cm (16.8%), PPRM (17.5%) and fetal distress (14.9%) (Zaini, et al., 2008). The reason for the lower rate was due to good general health status, which were healthy, younger age, non-smoker and fewer preexisting medical illness

Based on a case control study in Iran by Chythra R. Rao et al., in 2014, the prevalence rate of PTB was 5.1% and the most significant risk factors associated with PTB were history of previous PTB (OR =12.7, CI: 3.9-40.4, $p < 0.001$) and oligohydramnios (OR= 3.9, CI: 1.6-9.5, $p = 0.002$) (Chythra R. Rao, et al., 2014).

Considerably fewer studies have evaluated the association between gestational weight, maternal height, maternal age, racial, cultural, behavior and medical illness during pregnancy but have many contradictory results (Chythra R. Rao. et al, 2014; Zaini et al, 2008; Bernabe et al, 2004; Katz et al, 2003; Ip et al, 2010). These studies only evaluated the risk factors without stratifying them according to the clinical subtypes.

Alhaj et al in 2010 found that among 3240 live birth at Omdurman Maternity Hospital, 126 (3.8%) were live preterm birth with 19 % were induced and the rest were spontaneous PTB.

4.2 Risk Factor For Preterm Birth

It is estimated that approximately half the spontaneous PTB are associated with intrauterine infection, which triggers the maternal and fetal inflammatory reaction, and leading to the initiation of contraction pain and PTB. There are many studies which associate infections such as periodontal disease and bacterial vaginosis with PTB and PPRM. However, their results were inconclusive (C et al, 2011; Moutqun, 2003; Michalowicz et al, 2006; Bernabe et al, 2004).

4.3 Subtype Of Preterm Birth

PPROM has a high association with PTB. Leaking liquor is frequently occurs at term but when it occurs preterm it usually results in PTB. A study done by Devlieger R, et al., (2006), hypothesized that the similar infectious mechanisms that cause the loss of membrane integrity are also responsible for triggering the inflammatory process that lead to uterine contractility.

Study by Ip, et al., in Thailand (2010), concluded that maternal age, pre-pregnancy body mass index, prior history of PTB and no prenatal care were the risk factors identified for PTB and suggest heterogeneity in risk factors of PTB. Therefore the probable causes of PTB can be divided in three subclinical subtype; spontaneous PTB, PPRM and medically indicated PTB.

In Malaysia, the prevalence of PTB was 10% in 1998 and increasing about 12.3% in 2012 (Sim and Hong, 2008; Zaini et al, 2008). However, this number may not be real and the prevalence may keep increasing year by year due to increase in facilities and preventive measures and management protocols. Moreover, although the risk factors for PTB have been widely studied in European and North American population, but they have not been extensively characterized in Malaysian women particularly in Kelantan. Therefore, this study sought to evaluate the risks of PTB in association of maternal socio-demographics, behaviors, and medical characteristic among Malaysian women generally and Kelantanese women specifically.

4.4 Justification and Rationale Of The Study

By knowing the real prevalence and defining risk factors for prediction of PTB is a good reasonable goal for several reasons.

First, identification of at –risk women allows initiation of risk – specific treatment. Therefore, specific intervention can be applied on those risks. Finally, identification of risk factors might give important clues to identify the mechanisms leading to preterm birth.

OBJECTIVES

5.0 OBJECTIVES

5.1 General Objective

To determine the prevalence and risk factors of preterm birth in HUSM in January 2014 to December 2015.

5.2 Specific Objectives:

1. To identify the prevalence of preterm birth in HUSM.
2. To identify the risk factors of preterm birth in HUSM in the category of socio-demographic, previous pregnancy and reproductive characteristic and current maternal and prenatal pregnancy status.
3. To determine the distribution of preterm birth according to clinical subtype (causes) and gestational age of preterm birth.
4. To determine the significant association of preterm birth according to socio-demographic background, current maternal and prenatal characters and previous pregnancy and reproductive characteristics.

METHODOLOGY

6.0 METHODOLOGY

6.1 Materials And Methods

6.1.1 Study Design

A retrospective case – control study

- A case –control study using one control for each case of preterm birth 1st of January 2014 – 31st December 2015

6.1.2 Study Setting

Hospital Universiti Sains Malaysia

6.1.3 Study Population

Woman who delivered between fetal viability and before 37 weeks of gestation. Preterm delivery cases will be identified by tracing record via records office.

Controls is women who delivered at term (≥ 37 weeks of gestation) and randomly selected by tracing delivery record in records office of the first woman who give birth at term the same day the woman who has preterm birth. If the same day occurs more than 1 preterm birth, the next control group will be selected by tracing delivery record the second woman who gives birth at term in the same day.

6.1.4 Analytical Variable Specification

Preterm birth – the diagnosis of preterm birth was made by using the American College of Obstetricians and Gynecologists (ACOG) guidelines (Engle, 2006). Gestational age is based on the last menstrual period (LMP) or ultrasound examination. If both LMP and ultrasound dating (before 20 weeks gestation) are available and both agreed within 2 weeks (14 days), the former measurement will be used to assign the gestational age. If the two dates differed by more than 2 weeks, the ultrasound date will be used instead.

The precise definition of fetal viability however is still not specific to certain date. By WHO definition, defining fetal viability is from 22 weeks and the Royal College of Obstetrician and Gynaecologist (RCOG) said that fetal viability is from 24 weeks (Lumley, 2003) . Therefore, the propose range between 24 weeks to less than 37 weeks gestation for the definition of preterm birth seems reasonable for this study. In case the date is uncertain, a birth weight of 500 grams is taken to define the lower limit of viability (P.M. Dunn & Stirrat, 1984).

To consider the multiple risk factor in the etiology of preterm birth, categorization are done by divided the preterm birth cases according to the three clinical subtype previously described as spontaneous PTB, preterm pre-labour rupture of membrane (PPROM), and medically indicated PTB.

Spontaneous preterm birth (SPTB) cases are the women whose medical records indicated a doctor diagnosis of spontaneous onset of labour with intact fetal membranes and delivery before completion 37 weeks gestation.

Preterm pre-labour ruptures of membrane (PPROM) cases are those women whose medical records indicated a doctor diagnosis of rupture of fetal membranes prior to onset of labour and delivery before completion 37 weeks gestation.

Medically indicated preterm birth (MIPTB) cases are those women who delivered prior to 37 completed weeks of gestation as a result of medical intervention.

Preterm birth was categorized according to gestational age at delivery based on WHO guidelines (World Health Organization , 2012) as below;

1. Mild preterm birth >32 – 36 weeks 6 days
2. Very preterm birth 28-32 weeks
3. Extremely preterm birth < 28 weeks

6.1.5 Other Covariates –

Covariates considered in this study included

1. Maternal socio-demographic factors – maternal age, education level , employment status and marital status
2. Maternal and prenatal care characteristics – maternal pre-pregnancy body mass index (BMI), height, medical disorder; diabetes and hypertension during pregnancy and prenatal care onset or booking and infant gender.
3. Previous pregnancy and reproductive history – parity (number of previous pregnancies lasting >24 weeks gestation), previous preterm birth, previous caesarean section, previous miscarriage and previous stillbirth.

6.2 Study Participants

6.2.1 Inclusion Criteria

For cases:

1. All live birth either vaginally or by caesarean section occurred between 24 weeks to less than 37 weeks during study period delivered in HUSM
2. Singleton
3. Cephalic presentation

For control:

1. Live birth occurred ≥ 37 weeks either vaginally or by caesarean section delivered in HUSM during study period
2. Singleton
3. Cephalic presentation

6.2.2 Exclusion criteria

1. Miscarriage < 24 weeks by LMP or weight < 500 gm by ultrasound age
2. Stillbirth ≥ 24 weeks
3. Multiple pregnancy
4. Cervical cerclage
5. Pathology in uterine i.e., congenital anomaly of reproductive organ or uterine fibroid
6. Congenital fetus
7. Women with missing/ incomplete prenatal care record

6.3 Sample Size Determination

Objective 1 = Prevalence of Preterm Birth

The sample size was calculated using single proportion formula as below:

$$n = \left(\frac{Z\alpha}{\Delta}\right)^2 P(1 - P)$$

Anticipated population proportion (P) = 5.8 % (Chythra R. Rao, et al., 2014)

Absolute precision (Δ) = 0.05

$$Z = 1.96$$

$$P = 5.8\% = 0.058$$

$$n = \left(\frac{1.96}{0.05}\right)^2 0.058 \times (1 - 0.058) = 83.9 \gg 84 \text{ (sample)} + 16 \text{ (dropout)} = 100 \text{ each case and}$$

control.

Objective 2 = Risk Factors for Preterm Birth

For the risk factor, sample size is calculated using Power and sample size calculation program version 3.0.1 as below, using t- test for numerical variable and dichotomous for categorical variable

Po is probability of exposure among control group

Power = 0.8

$\alpha = 0.05$

m ratio = 1

Table from literature review for each categorical risk factor to get Po and P1

Based on previous study by Ip, et al., (2010),

Table 6.3.1: Sample Size According To Risk Factor According To Socio-Demographic And Behavior

Variable	Po	P1	α	1- B/Power	N	N+ 20% Dropout
Maternal Age < 20	0.34	0.64	0.05	0.8	42	50
Maternal Education (secondary school)	0.49	0.79	0.05	0.8	39	47
Marital Status (Not Married)	0.51	0.81	0.05	0.8	38	46
Employed During Pregnancy	0.49	0.79	0.05	0.8	39	47

**Table 6.3.2: Sample Size According To Risk Factors Associated With
Previous Pregnancy And Reproductive Characteristic**

Variable	Po	P1	α	1-B/Power	N	N+ 20% Dropout
Parity Nulliparous	0.47	0.77	0.05	0.8	40	48
Previous History Preterm Birth	0.12	0.42	0.05	0.8	33	39
Previous History Stillbirth	0.52	0.82	0.05	0.8	37	44
Previous History Miscarriage	0.13	0.43	0.05	0.8	34	41
Previous History Caesarean Section	0.23	0.53	0.05	0.8	40	48

Table 6.3.3 Sample Size According To Risk Factors Associated With Current Pregnancy Characteristics

Variable	Po	P1	α	1-B/Power	N	N+ 20% Dropout
Pre-Pregnancy Body Mass Index (BMI) <18.5	0.4	0.7	0.05	0.8	42	50
Maternal Short Stature <145cm	0.5	0.8	0.05	0.8	38	46
Gestational Age Starting Prenatal Care > First Trimester	0.22	0.52	0.05	0.8	39	47
Women With Hypertension	0.30	0.60	0.05	0.8	42	50
Women With Diabetes	0.42	0.72	0.05	0.8	42	50
Baby Gender	0.48	0.78	0.05	0.8	39	47

Objective 3 = Distribution of Preterm Birth According Clinical Subtype and Gestational Age

The sample size was calculated using single proportion formula as below:

$$n = \left(\frac{Z\alpha}{\Delta}\right)^2 P(1 - P)$$

Table 6.3.4: Sample Size According To Clinical Subtype Based On Previous Study By Howson, Et Al., (2012).

Clinical Subtype[23]	P	Each Sample Size + 20% Dropout
Spontaneous PTB	85.7% = 0.85	234
PPROM	5.3% = 0.053	93
Medically Indicated PTB	9% = 0.09	148

Table 6.3.5: Sample Size According To Gestational Age At Delivery Based On Previous Study By Beck, Et Al., (2010).

Gestational Age (Weeks)[24]	P	Each Sample Size + 20% Dropout
Mild >32 weeks	65.3% = 0.653	418
Very preterm (28-32)	29.3% = 0.293	382
Extremely preterm <28	5.4% = 0.054	95

Based on sample size calculation, sample size for preterm birth according to gestational age (mild preterm birth >32 weeks) is chosen due to the higher number for definite sample size in this study = 418 for each case and control data.