DSPACE

https://dspace.org/

Maternal risk factors for low birth weight at South rand hospital (Johannesburg)

Abdulsalam, Abdulrauf

2017
http://hdl.handle.net/10539/23257

Downloaded from a DSpace repository. https://dspace.org/

Maternal Risk Factors for Low Birth Weight at South Rand Hospital (Johannesburg)

Abdulrauf Abdulsalam

Student number 591222

A research report submitted to the Faculty of Health Sciences Witwatersrand University, Johannesburg in partial fulfilment of the requirements for the degree of Master of Medicine in Family Medicine

Supervisor: Dr Jimmy Agetta Akii

Co-supervisor: Prof Buchmann Ekhart

Johannesburg, South Africa

2017

DECLARATION

I, Abdulrauf Abdulsalam, declare that this research report is my original work. It is being submitted for the degree of Master of Medicine in Family Medicine at the University of Witwatersrand, Johannesburg. It has never been submitted for any degree or examination at this or any other university.

……

Abdulsalam Abdulrauf

10th day of March 2017

DEDICATION

To my Wife

Nafisat Jolade Abdulsalam

To my children

Neemat Eniola Abdulsalam

Abdulsamad Opeyemi Abdulsalam

Abdulqudoos Oladipupo Abdulsalam

ABSTRACT

Background: Low birth weight (LBW) is an important risk factor for infant developmental problems, morbidity and mortality. Low birth weight babies are twenty times more likely to die during the neonatal period than their normal weight counterparts. Although risk factors for low birth weight vary from one community to another, maternal risk factors for low birth weight in the South Rand Hospital (Johannesburg, Gauteng) catchment area have not been investigated. The **objective** of this study was to determine maternal risk factors for low birth weight in South Rand Hospital, Johannesburg.

Method: This 1: 1 matched case-control study was conducted on a total of 480 mothers who delivered babies at South Rand Hospital between 1 January 2013 and 31 December 2014. The cases were 240 mothers who delivered singleton term live LBW babies. They were matched with an equal number of controls.

Results: Conditional logistic regression showed that, no anaemia in the third trimester (OR=0.54, 95% CI= 0.30-0.99), immigration status (OR= 0.46, 95% CI= 0.25- 0.85) and four or more antenatal care clinic attendance (OR=0.36, 95% C.I= 0.12- 0.76) were protective factors, while smoking during pregnancy (OR= 8.69, 95% CI= 2.70-28.35) predisposes to delivering a LBW baby.

Conclusion: The results showed that smoking during pregnancy is a risk factor for LBW, while maternal third-trimester haemoglobin level of 11g/dl or more, immigrant status, and more than three ANC visits were protective factors for delivering LBW baby.

ACKNOWLEDGEMENT

Firstly, I thank Almighty God for His mercy and for making this research report come to fruition.

I thank my supervisor, Dr Jimmy Agetta Akii, for his guidance throughout the study. To my co-supervisor (Professor Buchmann Eckhart) thank you for your guidance, patience and understanding. Without the help of both of you, this report would not have been completed.

I am grateful to my wife and children for their support during my training as a registrar and the writing-up of this research.

I acknowledge the help from the school of public health for the statistical support. Thank you to Dr Michel Muteba and all the other statisticians that I consulted with at Philip Tobias building.

To all the nurses and the support staff working in the maternity ward of the South Rand Hospital, thank you very much. I appreciate your help and cooperation during this study. To the chief executive officer of South Rand Hospital (SRH), thank you for granting me the permission to conduct the study at the hospital.

Lastly, I thank Family Medicine department of Witwatersrand University for the opportunity to carry out his research.

Thank you all for making my MMed possible.

TABLE OF CONTENTS

TITLE PAGE I

DECLARATION I

DEDICATION II

ABSTRACT III

ACKNOWLEDGEMENT IV

TABLE OF CONTENTS V

LIST OF FIGURES VIII

LIST OF TABLES IX

ABBREVIATIONS X

GLOSSARY OF TERMS XI

CHAPTER 1 1

INTRODUCTION 1

1.1 BACKGROUND 1

LITERATURE REVIEW 4

2.1 DEFINITION AND INCIDENCE OF LOW BIRTH WEIGHT 4

2.2 AETIOLOGY OF LOW BIRTH WEIGHT: RISK FACTORS 6

2.3 MATERNAL RISK FACTORS FOR LOW BIRTH WEIGHT 6

2.3.1 MATERNAL SOCIO-DEMOGRAPHIC FACTORS 6

2.3.1.1 MATERNAL AGE 6

2.3.1. 1 MATERNAL MARITAL STATUS 7

2.3.1.3 EDUCATIONAL LEVEL 8

2.3.1.5 RACE 9

2.3.1.6 IMMIGRATION STATUS 10

2.3.1.7 PARITY 10

2.3.1.8 MISCARRIAGE 11

3.2 BEHAVIOURAL RISK FACTORS 11

2.3.2.1 ALCOHOL 11

2.3.2.2 SMOKING (CIGARETTE) 12

2.3.3 INFECTIVE MATERNAL RISK FACTORS 13

2.3.3.1 HUMAN IMMUNODEFICIENCY VIRUS AND OTHER CHRONIC INFECTIONS 13

2.3.4 NON-INFECTIVE MATERNAL RISK FACTORS 14

2.3.4.1 MALNUTRITION 14

2.3.4.2 HYPERTENSION 15

2.3.4.3 ANTENATAL CARE 16

2.4 RISK FACTORS FOR SGA AT TERM 16

2.5 RESEARCH QUESTION 17
2.6 STUDY HYPOTHESIS 18
2.6.1 NULL HYPOTHESIS 18
2.7 AIM OF THE STUDY 18
2.8 OBJECTIVES 18
CHAPTER 3 19
METHODOLOGY 19
3.1 STUDY DESIGN 19
3.2 STUDY SITE 19
3.3 STUDY POPULATION 21
3.4 STUDY SAMPLE 21
3.5 INCLUSION CRITERIA 22
3.6 EXCLUSION CRITERIA 22
3.7 SELECTION OF STUDY PARTICIPANTS 22
3.7.1 IDENTIFICATION OF CASES 22
3.7.2 SELECTION OF CASES 23
3.7.3 MATCHING OF PARTICIPANTS 23
3.7.4 IDENTIFICATION AND SELECTION OF CONTROL 23
3.7.5 FILE RETRIEVAL 26
3.8 DATA COLLECTION 26
3.9 MEASURING TOOL 26
3.10 DATA ANALYSIS 27
3.11 PILOT 28
3.12 ETHICAL CONSIDERATIONS 28
3.13 FUNDING 29
CHAPTER 4 30
RESULTS 30
4.1 STUDY POPULATION 30
4.1.1 SAMPLE SELECTION 30
4.2.1 DISTRIBUTION OF STUDY PARTICIPANTS BY MATCHING VARIABLES 30
4.2.2. MATERNAL SOCIO-DEMOGRAPHIC AND BEHAVIOURAL CHARACTERISTICS 31
4.2.3 DISTRIBUTION OF MATERNAL CLINICAL FACTORS BETWEEN GROUPS 33
4.3 INFERENTIAL STATISTICS 36
4.3.1 COMPARISON OF MATERNAL RISK FACTORS BETWEEN CASES AND CONTROL 36
4.3.1. REGRESSION ANALYSIS 38
CHAPTER 5 42

DISCUSSION 42
5.1 METHODOLOGY 42
5.3 ASSOCIATION BETWEEN VARIABLES AND REGRESSION ANALYSIS 43
5.3.1 SOCIO-DEMOGRAPHIC AND BEHAVIOURAL RISK FACTORS 43
5.3.1.1 AGE OF MOTHERS 43
5.3.1.2 RACE 43
5.3.2.3 MARITAL STATUS 44
5.3.2.3 EMPLOYMENT 45
5.3.2.4 IMMIGRATION 46
5.3.2.5 PARITY 46
5.3.2.6 SMOKING (CIGARETTE) 47
5.3.2.7 ALCOHOL 48
5.3.3 MATERNAL CLINICAL RISK FACTORS 49
5.3.3.1 TIMING OF ANC BOOKING 49
5.3.3.2 NUMBER OF ANC ATTENDANCE 50
5.3.3.3 MATERNAL HAEMOGLOBIN LEVEL 50
5.3.3.3.1 HAEMOGLOBIN LEVEL AT FIRST ANC VISIT 50
5.4.14 HAEMOGLOBIN LEVEL IN THE THIRD TRIMESTER 51
5.3.3.4 HYPERTENSIVE DISORDERS OF PREGNANCY 52
5.3.3.5 HIV STATUS OF MOTHERS 52
5.3.3.6 AVERAGE MATERNAL WEIGHT GAIN PER WEEK AFTER THE FIRST TRIMESTER 53
5.3.3.7 MISCARRIAGE 54
CHAPTER 6 55
CONCLUSIONS AND RECOMMENDATIONS 55
6.1 CONCLUSIONS 55
6.2 RECOMMENDATIONS 55
6.3 LIMITATIONS 56
APPENDIX 1: ETHICS CLEARANCE CERTIFICATE 57
APPENDIX 2: CERTIFICATE OF APPROVAL BY THE CEO OF SR 58
APPENDIX 3: INFORMATION EXTRACTION FORM 59
APPENDIX 4: GAUTENG PROVINCIAL GOVERNMENT ANC CARD 63
APPENDIX 5: MATERNAL CASE RECORD FILE 65
APPENDIX 6: CASE/CONTROL RECORD 68
REFERENCES 69

LIST OF FIGURES

Figure Page

1.1 Map showing the sub-districts of Johannesburg metropolitan health district….20
1.2 Flow chart showing case selection process……..……..…..25

LIST OF TABLES

Table Page

4.1 Distribution of case and controls as per matched variables……..31

4.2 Distribution of maternal socio-demographic and behavioural Characteristics……..…32

4.3 Distribution of maternal clinical factors……....34

4.4 Comparison of numerical variables between cases and controls……...36

4.5 Difference between numerical exposure variable among cases and control…..37

4.6 McNemar Chi-square test for binary categorical variable and LBW…… 37

4.7 Bivariate conditional logistic regression…….……39

4.8 Conditional logistic regression……....41

ABBREVIATIONS

ADH……Adenosine Dehydrogenase

ANC ……...Antenatal Care

BBA……Born Before Arrival

BTT…….Birth To Ten

CHBH…….Chris Hani Baragwanath Hospital

CHC……Community Healthcare Centre

DHIS……...District Health Information System

FAE……..Foetal Alcohol Exposure

FAS…….....Foetal Alcohol Syndrome

HIV……...Human Immunodeficiency Virus

HREC……...Human Research Ethics Committee

IUFD……....Intra Uterine Foetal Death

IUGR……Intra-uterine Growth Restriction

LBW…….....Low Birth Weight

LGA……..Large for Gestational Age

LNMP……...Last Normal Menstrual Period

MOU…….....Midwife Obstetric Unit

PHC……...Primary Health Care

PPIP……...Perinatal Problem Identification Programme

SGA……...Small for Gestational Age

USA……...United States of America

UTI…….....Urinary Tract Infection

WHO…….World Health Organization

GLOSSARY OF TERMS

Low birth weight: Baby weighing less than 2500g at birth. Weight should ideally be taken within an hour of delivery before postnatal weight loss occurs.

Term pregnancy: A pregnancy that has duration of at least 37 completed weeks

Preterm birth: Baby delivered before 37 completed weeks of gestation.

Intra uterine growth restriction: This refers to a situation whereby a foetus did not reach its growth potential because of genetic and/or environmental factors.

Small for gestational age baby: Birth weight less than 10^{th} centile of gestational age for sex of the baby.

Primary health care: This is a health facility that serves as the entry point into the health care system. It offers basic essential health care services.

Community health centre : This is a health centre that is open 24 hours a day and seven days a week. It offers a wide range of primary health care services including accident and emergency and midwifery services, but not surgery under general anaesthesia.

District hospital: This is a health facility which offers a range of inpatient and outpatient services that are mostly within the scope of a general medical practitioner. It has a functional operating theatre where operations are regularly performed under general regional or general anaesthesia.

Weight gain per week: This is the weight gain by a pregnant woman during pregnancy divided by the number of weeks over which the weight gain occurred.

CHAPTER 1

INTRODUCTION

1.1 Background

Low birth weight (LBW) is defined by the World Health Organization (WHO) as a birth weight of less than 2500g.[1] Etiologically, it could result from premature interruption of pregnancy (preterm) and/or intra-uterine growth restriction (IUGR).[2] LBW may be associated with foetal exposure to unfavourable maternal conditions during pregnancy, such as smoking, alcohol consumption, malnutrition and inadequate antenatal care.[3] LBW is a potentially preventable public health issue common in low and middle-income countries.[4] Statistics show that every ten seconds, an infant dies in low or middle-income countries of causes attributable to LBW.[5] Children born with LBW have schooling and a variety of health problems which can limit their physical, cognitive and mental development. LBW babies are twenty times more likely to die in their first year of life than their heavier counterparts.[6] Adults born with low birth weight have a higher risk of developing chronic illnesses like systemic arterial hypertension, non-insulin dependent diabetes mellitus, coronary artery disease and stroke.

Factors predisposing to LBW among term babies can be classified into maternal, foetal and genetic factors. Maternal factors can be further classified into, socio-demographic and clinical factors. Maternal socio-demographic factors include age, race, educational level, smoking, alcohol, marital status, immigration status and employment status. Maternal clinical factors include nutritional status before and during pregnancy, infections during pregnancy, timing of and number of antenatal care (ANC) visits and chronic illnesses like diabetes mellitus and systemic hypertension.

This study was conducted to investigate the following maternal factors; Human Immunodeficiency Virus (HIV) infection, antenatal care attendance, systemic arterial hypertension, immigration status, race, smoking, alcohol consumption and employment status as explanatory variables for delivery of LBW baby at term amongst women who delivered at South Rand Hospital. Mothers with chronic conditions like diabetes mellitus, epilepsy, asthma, and cardiac diseases are usually referred to a higher level of care for their deliveries. These conditions were not investigated as explanatory variables for delivery of LBW baby in this study.

1.2 Rationale for the study

The incidence of LBW in a society is often used as a primary indicator of children's health in the society at a specified time.[7] The WHO uses LBW rates along with maternal nutritional status as primary indicators of public health and prenatal care.[8]

Incidence of Low birth weight in Gauteng province increased from 11% to 16% over three years (2008-2011).[9] It is worrying that this rate which predicts new-born health, their ability to survive and the quality of antenatal care given to pregnant women is increasing at such an alarming rate.[3]

Evidence from Anglo-Saxon communities suggests that LBW babies have more adverse short and long term outcomes compared to normal birth weight babies. They have a high neonatal treatment cost, high probability of mortality in infancy and lower educational attainment and labour market outcomes.[10] A high rate of low birth weight babies increases the burden of care on the healthcare system.[11] For example, due to a high burden of babies with LBW and a limited number of mechanical ventilators and other resource constraints, infants weighing less than 1000 grams are not offered mechanical ventilation at a referral hospital in Johannesburg.[12] Similarly, there is a quota restriction on the use of exogenous surfactant for preterm LBW babies who needed surfactant because of resource constraints.

Low birth weight babies spend more days on admission in the hospital especially in their first years of life than their normal birth weight counterparts.[13] An average cost of admission and treatment per LBW baby for the first two weeks of life at a government facility in the Eastern Cape was estimated to be R12, 000 in 2008.[14] In America, neonatal cost for a new-born weighing between 500 – 700g was $224 400 while the cost for new-born weighing more than 3000g was $1000.[15]

Controversies still exist on the determinants of LBW. This is because of the difficulty in finding factors that are frequently associated with LBW in different communities. This difficulty arose because different social realities operate in different communities.[3] Sub-Sahara Africa has a limited evidence on neighbourhood factors for LBW.[16] The researcher while working at South Rand Hospital observed an increase in the number of LBW babies delivered at the hospital, but literature review showed that there was no published study which investigated maternal risk factors and low birth weight in SRH catchment area. The leaves a knowledge gap about the maternal risk factors for low birth weight among women who delivered at SRH. These factors may be context-specific. Therefore, this study was conducted to identify local maternal risk factors for low birth weight that may be amenable to policy decisions.

This study community may have some peculiarity in terms of immigration status and access to antenatal care and delivery. Immigration status is a peculiarity because of the then policy decision made by the Gauteng Department of Health requiring non-South African patients to pay a deposit fee of R8000 before obstetric services were rendered at SRH.[17] Little is known about the effect of immigration status on low birth weight.[18] This type of study may help to determine the effect of maternal immigration status on the birth weight of their babies in this community. It may also help in the development of context specific interventions to reduce the rate of LBW. The birth to twenty research programme of the University of Witwatersrand did not specifically look at risk factors for low birth weight.[19] Also, the Perinatal Problem Identification Programme (PPIP) only collect detailed information on mothers whose babies died.[10] For LBW babies, only general count data are captured and there is no additional information on the types of risks the mothers were exposed to during pregnancy.

CHAPTER 2

LITERATURE REVIEW

A literature review on maternal risk factors for low birth weight was carried out using the following databases; Google Scholar, PubMed, Cochrane, Medline, CINAHL and Science Direct. Electronic repositories of research reports of South African Universities were searched for relevant studies. Search terms used included, low birth weight, small for gestational age, preterm, term, maternal factors, pregnancy outcome, risk factors, developing, developed, South Africa, immigration, meta-analysis, case-control and regression. Reference lists of the relevant studies were also searched. This literature search showed that low birth weight has been a public health concern for a long time and that maternal factors for low birth weight may vary from one region to another. However, there is a paucity of published research in South Africa specifically on maternal risk factors for low birth weight. No studies have been conducted in a level one hospital in South Africa. Among the published studies, none of them used a matched case-control design.

2.1 Definition and incidence of low birth weight

Birth weight is the first weight of a new-born obtained soon after delivery.[20] Ideally, it should be measured within the first hour of life, before postnatal weight loss occurs. In 1967, the WHO defined an infant weighing less than 2500 grams at birth as a low birth weight baby.[21] This practical cut-off point is based on epidemiological observations that new-born babies weighing less than 2500 grams at birth are approximately twenty times more likely to die during the infancy period than heavier babies.[22] This practical cut-off point was also set for international comparison to be made.

The birth weight of a baby is determined by both the duration of the pregnancy and the rate of foetal growth during the pregnancy. Therefore, LBW could result from, delivery before thirty seven completed weeks of pregnancy (preterm) and/or a small

for gestational age (SGA) baby. A Small for Gestational Age baby is a baby whose weight at birth falls below the tenth centile for its gestational age and sex.[23] Causes of SGA baby could be intrauterine growth restriction (IUGR) and/or a genetic factor. About 70% of LBW babies are born preterm, and 30% are termed SGA (37 or more weeks of gestation).[1]

The worldwide incidence of LBW is 15.5%, but country-specific incidence rates vary from one country to another.[22] It varies from a mean value of 25% in India to 7.6% in the USA, 5.6 % in Scandinavian countries and 6.1% in the United Kingdom. South Central Asia has the highest incidence rate of 27% and this accounts for more than half of LBW babies born worldwide. South and Central America have an average LBW incidence of 10%, the Caribbean 14%, these are about the same values as sub-Saharan Africa (13-15%).

Low birth weight could be classified into preterm SGA, preterm AGA (appropriate for gestational age), term SGA and term AGA. Since LBW in low and middle-income countries is mainly due to IUGR, this study is methodologically about maternal risk factors for term SGA. This is done to specifically identify maternal risk factors for this sub-set of LBW babies. The incidence of SGA in Brazil is 13.1%, 15.8% in Tanzania and 8.4% among South Indian women.[24] Sub-Sahara Africa has SGA at term incidence rates of 23.5%.[25]

Over twenty million babies are born annually with LBW.[22] Ninety-six percent of LBW babies are born in low-income countries. In low-income nations, the incidence of LBW is underestimated because some births take place outside the healthcare facilities where birth weights cannot be measured and documented. Sub-Sahara Africa accounts for the births of three million LBW babies annually. Literature shows that many low-income nations have a LBW incidence rate that is above the internationally recommended cut-off levels.

2.2 Aetiology of low birth weight: risk factors

As a result of the profound health and social consequences of low birth weight, causes of LBW have been the focus of multiple investigations over the last few decades.[26] Causes of LBW could be iatrogenic (early induction of labour or caesarean section), multiple pregnancies, infections, chronic conditions such as diabetes mellitus and arterial systemic hypertension. These factors can be grouped into maternal and foetal factors. This literature review focused on maternal factors for LBW in general and specifically SGA at term.

2.3 Maternal risk factors for low birth weight

Some maternal factors have been associated with low birth weight. They include socioeconomic, clinical, environmental, genetic and behavioural factors. In this literature review, maternal socio-demographic, clinical and behavioural factors will be discussed in line with the aim of the study.

2.3.1 Maternal socio-demographic factors

2.3.1.1 Maternal age

Pregnancy outcome such as birth weight is less satisfactory among adolescent mothers and women older than 35 years.[27] However, controversy still looms as to whether age itself independently determines the intrauterine growth rate or the duration of gestation. The biological plausibility that incidence of LBW will be higher in extremes of maternal reproductive ages has been supported by epidemiological studies. These epidemiological studies showed that in the lower extreme of maternal age (less than 19 years), it is thought that pregnancy outcome could be a result of maternal social deprivation leading to the observed effect and not as a manifestation of maternal age itself.

Most adolescent mothers are single with little or no income and poor or no prenatal care. They are often involved in illicit drug use and they are usually late in seeking antenatal care because of the unplanned nature of their pregnancies.[12] As a result of these factors, they are more likely to deliver a LBW baby. In addition to this, the blood supply to the cervix and uterus are yet to fully develop in adolescent mothers, this leads to poor blood supply to the developing foetus. Nutritional competition between the developing adolescent mother and her foetus has also been suggested as a possible aetiology for delivery of low birth weight babies by these mothers.[27] In America, the most important predictor of LBW in the adolescent age group is inadequate prenatal care and an adverse obstetric history.[28]

It is believed that pregnancy at the age of 35 years and above is associated with higher occurrences of pregnancy complications such as arterial systemic hypertension and diabetes mellitus than in younger women. Higher maternal age may also be associated with high use of artificial reproductive techniques which may contribute to higher rates of preterm births and LBW.[29] Some authors suggest that the risk of LBW in mothers over 35 years is related not to maternal age itself, but to other processes like arterial systemic hypertension, diabetes mellitus and increased atherosclerotic disorders at myometrium level which are more common among older women than younger women.[12] All the above conditions increase the risk of delivering a LBW baby. Most studies agree that age is a risk factor for low birth weight.

2.3.1.2 Maternal marital status

Marital status or cohabitation is closely related to socioeconomic status. In high-income countries, cohabitation is independent of income, occupation and education status. Most of the time, cohabitation reflects life-style-based choices among people of middle and upper social classes. Any effect of cohabitation on the rate of intrauterine growth and/or duration of pregnancy might occur in mothers through a psychological pathway (e.g. stress) independent of their socio-economic status.

Studies have shown that being married has a protective effect on LBW.[12]When married women were separated from their partners in subsequent pregnancies; they had a 1.4 increase in relative risk of delivering LBW babies compared to women who were still married. Among women who became married after delivery in a single marital state, the relative risk of delivering a LBW baby decreased by 0.8. This finding was supported by a similar study in Nigeria,[30] but a study conducted in Botswana report that the effect of being married disappeared when a control group was introduced. Premature delivery was 1.8 times more common for unmarried mothers and this effect remained even when control groups were introduced.[31]

A meta-analysis by Kramer on LBW stated that evidence for marital status as an independent determinant of LBW is inconclusive, although, contributory studies to this conclusion were all conducted in developed countries.[26] There is a paucity of local study that investigates effects of marital status on birth weight. A study in Cape Town by Oliver reported that single mothers were more likely to deliver a LBW baby with an odds ratio of 1.73.[32] The basis for the protective effect of marriage may be due to social, psychological, emotional and financial support offered by marriage partners. Married mothers also tend to have better health status compared to unmarried mothers. Further research is needed to understand the mechanism of the effect of marital status on pregnancy outcome, such as birth weight.

2.3.1.3 Educational level

Some studies have suggested that there is an important relationship between birth weight, prematurity and maternal educational level.[21] Mothers with no education are 1.4 times more likely to give birth to LBW babies than those with at least secondary education.[17] In China, low maternal educational level is reported to increase the incidence of LBW by up to 38%.[33] In contrast, the level of maternal educational attainment does not have a significant association with birth weight in Jamaica. This finding may be due to the fact that the majority of women in Jamaica have a primary education and having a higher education without a higher income has a limited protection on the likelihood of delivering a LBW baby.[34] In the USA, above a certain level of maternal education, the likelihood of delivering a LBW baby decreases with

increasing maternal education levels.[13] The paternal education level may also influence birth weight. There is a paucity of published South African studies that investigate the influence of maternal and paternal educational levels on and LBW.

2.3.1.4 Employment and income status of parents

Both maternal employment and unemployment can influence the likelihood that a mother will deliver a LBW baby. The mechanism through which unemployment predisposes babies to LBW is poverty. Poverty can cause maternal malnutrition, anaemia and infection before and during pregnancy. Employment in a strenuous job can also incline a baby to have LBW through preterm labour and antepartum haemorrhage. Night work during pregnancy may prolong pregnancy and reduce foetal growth.[11] A local study conducted with a population with similar employment statuses showed that the higher the income, the less likely the chances were of delivering a LBW baby.[18]

2.3.1.5 Race

Evidence suggest that black women have a higher risk of delivering a LBW baby than their white counterparts.[21] It is, however, difficult to find studies with a comparison across racial groups and with stratification by socioeconomic class. Investigators who focused on this area have concluded that genetic and environmental factors have a joint influence on low birth weight and it is difficult to isolate the effect of one from the other. In a study in Texas, USA, race was found to be a significant predictor of LBW. In that study, African-Americans were four times more likely to have a LBW baby compared to Euro-American mothers.[35] A study in the Eastern Cape by Ilunza supported the postulation that race is a significant factor for low birth weight.[14]

2.3.1.6 Immigration Status

Immigrant mothers seem to be at risk of adverse pregnancy outcomes, although there is a variation on the reported outcome from studies conducted in different high-income countries. The inconsistency in the results could be due to, different maternal countries of origin, the available social support in the host country and the outcome variables of interest. The perinatal health of immigrant mothers is sometimes found to be both better and worse than that of mothers who are citizens by birth.[35] A number of studies in United State of America (USA) reported that immigrant mothers have better pregnancy outcomes compared to native mothers despite their socio-economic status. Other studies also stated that the strength and direction of the association between the immigration status of mothers and low birth weight depend on the birth place of the mother and her socio-economic status. A study conducted in Belgium reported that being an immigrant has a protective effect on the likelihood of delivering a LBW baby on women with low a socio-economic status than women with a higher socio-economic status.[36]

2.3.1.7 Parity

Generally, pregnancy outcomes in terms of LBW is believed to be more favourable for multiparous women than primiparous women, but grand multiparity is believed to constitute a risk to the baby.[21] Investigating the effect of parity on low birth weight is however very difficult because of various confounding factors, such as the age of mother, the birth interval, and the mothers socio-economic status. In his review, Javier reported that most studies consider parity as a risk factor for low birth weight and that studies which failed to show a relationship between parity and LBW had small sample sizes.

2.3.1.8 Miscarriage

Spontaneous miscarriage overlaps with preterm delivery. The distinction between a late second-trimester miscarriage and prematurity is progressively blurring because of the increasing viability of infants delivered before 28 weeks. The effects of a prior history of second-trimester miscarriage may be the same as that of a prior history of a premature delivery.[26] Spontaneous miscarriages in previous pregnancies might affect a current pregnancy through a prior use of dilatation and curettage for the removal of retained products of conception. Cervical dilation could lead to cervical incompetence which predisposes a woman to preterm delivery in subsequent pregnancies. Cervical dilatation is usually more likely following a dilatation and curettage compared to a vacuum extraction. So, the number cervical dilation and curettages also play a role in the development of cervical incompetence. Prior history of a miscarriage does not affect intrauterine growth. Uterine surgical procedures may increase the chances of faulty implantation which may lead to subsequent placenta Previa and increase the risk of preterm births.[29]

3.2 Behavioural risk factors

2.3.2.1 Alcohol

After smoking, alcohol is the second most commonly investigated substance in relation to pregnancy outcome.**Error! Bookmark not defined.** Alcohol consumption by p regnant mothers may lead to foetal alcohol spectrum disorders; foetal alcohol syndrome (FAS), foetal alcohol effects (FAE) and alcohol-related neurodevelopmental disorders. Maternal alcohol consumption during pregnancy may adversely affect intrauterine growth.[26] The exact mechanism through which alcohol mediates its effect is not clear. Proposed theories include the permeability of foetal placental to ethanol leading to foetal exposure to the maternal level of alcohol and acetaldehyde. Acetaldehyde is a by-product of alcohol metabolism that is toxic to the foetus. Alcohol also predisposes to LBW through decreased incorporation of amino acids into protein and foetal hypoxia.

In South Africa, 11% of pregnant mothers consume alcohol at a level that are considered harmful to the foetus. This number varies from one socio-cultural group to another. Five to 10 percent of babies exposed to alcohol in utero will develop full-blown foetal alcohol syndrome, FAS.[13, 11] Development of FAS depends on the quantity of alcohol consumed by the mother and the gestational age of the foetus at the time of maternal alcohol consumption. Effects of alcohol consumption are worse when it is consumed in the first trimester. Ten percent of children of moderate alcohol drinkers will develop FAS. Most studies reported that maternal alcohol consumption during pregnancy has a detrimental effect on the intrauterine growth of the foetus. Kramer reported two studies that did not find any association between LBW and alcohol consumption. In one of these studies which failed to show an association, only 2.8% of the participants consumed more than two drinks per day. This small number of mothers who consumed more than two drinks per day significantly reduced the power of the study. This does not mean that there is a totally safe threshold level of alcohol consumption in pregnancy.[26] Alcohol intake is the second most significant risk factor for LBW in the Eastern Cape.[14] Cape Town has the highest prevalence of FAS in the world, with 40-46% per 1000 children aged 5-9 years.

2.3.2.2 Smoking (cigarette)

A pregnant woman's exposure to tobacco smoke could either be by maternal smoking or by exposure to smoke from other people, this is known as environmental tobacco smoke. Cigarette smoke of any kind can adversely affect the foetus.**Error! Bookmark not d efined.** The effect of maternal cigarette smoke was investigated in this study and it was the focus of this sub-section of the literature review. Cigarettes are the most commonly used of all the drugs that can affect the foetus.[12] Maternal smoking during pregnancy affects intrauterine foetal growth and duration of gestation, in a number of divergent ways.[26]

Carbon monoxide produced from cigarette smoke interferes with oxygen delivery to the foetus by shifting the oxygen-haemoglobin dissociation curve to the left. This results in less oxygen delivery to foetal tissue at a given partial pressure of oxygen.

Also, nicotine, a constituent of cigarette smoke, is an appetite suppressant and it is believed to increase maternal catecholamine levels. This leads to vasoconstriction of uterine vessels and reduction in blood flow to the developing foetus.[25] Tobacco smoke is also known to contain cyanide compounds which interfere with the foetal oxidative metabolism. Harmful substances may be found in the gametes of smokers even before conception. Smoking also predisposes the foetus to antepartum haemorrhage, especially placental abruption.[11] Even though there are serious consequences because of smoking during pregnancy, 25% of pregnant women who smoke at conception continue to smoke during pregnancy.

Most studies have demonstrated a temporal and a dose-response relationship between smoking during pregnancy and the delivery of a LBW baby.[26] Two studies which failed to uphold this position had small sample sizes. The effect of smoking depends on the period of gestation that the mother smoked, worse effects were noted when maternal smoking occurred in the third trimester. A mean maternal weight loss of 0.5 kg during pregnancy in women who smoke a pack of cigarettes a day has been reported. Maternal tobacco use during pregnancy results in a 70-250g reduction in birth weight. Passive smoking could reduce birth weight by 25g. Cessation of smoking before the third trimester leads to a reduction in the incidence of LBW. Local studies in the Eastern Cape and Cape Town both reported smoking as a significant risk factor for LBW.[14]

2.3.3 Infective maternal risk factors

2.3.3.1 Human immunodeficiency virus and other chronic infections

A substantial number of micro-organisms are able to cross the placenta and infect the developing foetus.[21] Foetal infection with some organism at a critical moment of foetal development may result in IUGR. The earlier the infection occurs during pregnancy the more serious its effects are on the baby. Microbial agents associated with foetal growth abnormality include Rubella, Toxoplasmosis, and the Herpes Simplex virus. There is a paucity of local studies on maternal HIV positive status as a

risk factor for delivery of low birth weight babies. A study in rural South Africa conducted before the advent of antiretroviral therapy in Government hospitals sought to investigate maternal HIV infection and its association with small for gestational age infants.[37] Using a prospective cohort study design, the study concluded that maternal HIV infection increases the risk of SGA, but not preterm births. A study at Chris Hani Baragwanath Hospital in Johannesburg looked at the outcome of very low birth weight babies born to HIV positive mothers.[38] This retrospective cross-sectional study concluded that the mortality rate for babies with a birth weight of less than 750g was 100%. The results revealed no major differences in the morbidity and mortality between HIV-exposed and HIV-unexposed newborns of a similar weight category. Given the country's HIV prevalence, more local studies are needed to investigate the effect of maternal HIV-positive status on LBW.

2.3.4 Non-infective maternal risk factors

2.3.4.1 Malnutrition

The nutritional status of both parents contributes to the birth weight of the baby. A mother's nutritional status contributes more to the birth weight of their babies than the father's nutritional status.[14] This finding is supported by studies which showed a correlation in birth weights between half-siblings of the same mother but not of the same father. This is due to a greater contribution from maternal genetics and the environment than paternal contributions. Maternal caloric intake and fat stores are the main energy source for foetal energy requirements. Foetal growth cannot occur without an adequate source of nitrogen and essential amino acids. It is therefore expected that maternal weight gain during pregnancy influences intrauterine foetal growth.

The effect of malnutrition on the birth weight of babies depends on the gestational age when the macronutrient deficiency occurred.[26] A decrease in birth weight was not observed in neonates of mothers who suffered malnutrition during the first or second trimester. A similar finding was observed during the Dutch famine, where a 50%

reduction in maternal energy intake in the first and/or in the second trimester was associated with an increase in placental weight but birth weight was unchanged. Maternal undernutrition in the third trimester affected both the placenta and the birth weight.

The nutritional status of the mother before and during the pregnancy is critical in predicting the birth weight of the baby.[39] The mechanism through which maternal under-nutrition affects foetal weight is by influencing the availability of substrates needed for foetal development. Foetal growth cannot occur without essential amino acids.[20] According to the WHO, maternal under nutrition contributes more than 50% to LBW in developing countries.[24]

In Cape Town, malnutrition has been shown to be a significant risk factor for LBW with a relative risk of 1.6.[5] Maternal average weight gain per week during pregnancy, haemoglobin level during pregnancy or oral iron intake is often used as a measure of maternal nutritional level during pregnancy. Studies that had a bearing on the impact of iron intake or anaemia on intrauterine growth and duration of gestation were either methodologically weak or were not carried out in developing countries.

2.3.4.2 Hypertension

The incidence of hypertensive disorders of pregnancy varied widely across regions with an average incidence of 10%.[11] Evidence shows that hypertensive disorders of pregnancy are associated with IUGR and LBW. This effect is mediated through a reduction in the uteroplacental circulation. Currently, it is also believed that there is a pathological increase in the thromboxane/prostacyclin index due to the deficient trophoblastic production of prostacyclin.[12]Through this mechanism, the production of prostacyclin is associated with asymmetric IUGR. In a study in the Eastern Cape, hypertensive disorders of pregnancy were ranked third among risk factors for LBW.[11]

Population-based studies from different countries have shown that chronic hypertension is one of the most common medical conditions in pregnancy.[40] It is associated with increased risk of SGA. Small for gestational age baby is more common when there is supper-impose pre-eclampsia (48%) compared to 21% with chronic hypertension alone.

2.3.4.3 Antenatal care

Antenatal care attendance by pregnant women could have a positive impact on the duration of gestation and intrauterine growth through a number of mechanisms. This could be by early identification and treatment of pregnancy complications.[26] It could also have an impact on the rate of LBW by modification, reduction or elimination of adverse maternal factors. The timing of the first ANC attendance also plays a major role because the effects of some pregnancy complications on birth weight could be mitigated if detected early. Observational studies reported a strong association between late booking (first ANC visit) and preterm births. In the USA, it was observed that giving African American Medicaid encourages mothers to seek early prenatal care, reduces the occurrence of LBW in those who received the Medicaid than in those who did not.[41] Less than three antenatal visits are associated with preterm births and LBW.

2.4 Risk factors for SGA at term

Of the135 million babies born in low and middle-income countries in 2010, 22% were term-SGA, 8% were preterm-AGA, and 2% were preterm- SGA. The relative risk for neonatal mortality for term-SGA was 2.4, 8 for preterm-AGA, and 15 for preterm-SGA.[42]

Pathophysiology of SGA is multifactorial and its effect is mediated through a complex of interactions between socio-demographic, clinical and behavioural

factors.[43] The socio-demographic factors include race, marital status, age and employment status. Obstetric factors include parity, history of previous preterm births, stillbirths or abortions, being a SGA mother and short or long interpregnancy intervals. Chronic medical conditions like arterial systemic hypertension, diabetes mellitus, abnormal placentation, chronic kidney disease, thyroid disorders, autoimmune disorders and urinary tract infections are also known to be risk factors SGA. Maternal health habits during pregnancy like smoking, alcohol consumption and nutritional intake also influence the delivery of SGA babies at term. Maternal ANC attendance, weight gain during pregnancy and the use of assisted reproductive techniques are risk factors for SGA at term.

Some of the factors listed above as risk factors for SGA at term are also factors for the other sub-sets of LBW categories. Late ANC attendance appears to be a more specific risk factor for SGA at term while socio-economic status appears specific for preterm-AGA. Maternal age of less than 16 years is a risk for term-SGA and preterm-AGA. Short maternal stature and being the first born is a risk factor for term-SGA, preterm-SGA and preterm-AGA.[42]

2.5 Research question

What are the maternal risk factors associated with the delivery of low birth weight babies among pregnant women who delivered live term babies at South Rand hospital between 1 January 2013 and 31 December 2014?

2.6 Study hypothesis

2.6.1 Null hypothesis

There is no difference in maternal risk factors under study between mothers who delivered live term LBW babies and those who delivered live term babies weighing 2500 grams or more at birth at SRH.

2.7 Aim of the study

To compare maternal risk factors for low birth weight of babies among women who delivered live term LBW babies and those who delivered term babies weighing 2500 grams or more at South Rand hospital.

2.8 Objectives

1. To describe the socio-demographic characteristics of mothers who delivered live, term babies at SRH between 1 January 2013 and 31 December 2014.

2. To compare the frequencies of maternal risk factors for low birth weight among women who delivered, live, term, LBW babies at SRH, in the study period and those who delivered, term, live babies, weighing 2500 grammes or more at birth at SRH in the study period.

3. To establish whether there is any association between the maternal risk factors under study and low birth weight.

CHAPTER 3

METHODOLOGY

3.1 Study design

This was a retrospective 1:1 matched case-control study.

3.2 Study site

This study site was South Rand Hospital, a level one district hospital located in sub-district F of the Johannesburg metropolitan health district. It has a total of 314 beds, two delivery suites and twenty postnatal beds. It serves a catchment population of about 450,000.[44] Majority of the users of this facility are people of low socioeconomic status and black race, the rest were from Indian, Coloured, and White racial groups. There is also a number of immigrants using this facility. This catchment population may compare to some of the referenced populations in the literature review.

The study was conducted at the postnatal ward (ward 2) of South Rand Hospital. This ward is located on the ground floor, in the west wing of the hospital. According to information contained in the birth register, SRH's average annual delivery is 3000. It is the referral hospital for all the surrounding clinics. SRH currently refers patients to Charlotte Maxeke Johannesburg Academic Hospital, a level three hospital. Obstetric referrals to Charlotte Maxeke Johannesburg Academic Hospital are due to number of reasons, such as, anticipated preterm births with immature foetal lungs, pre-eclampsia, eclampsia, or where there is a need for intensive neonatal care. When this study was conducted, the obstetric department was managed by an obstetrician, family physicians, family medicine registrars and medical officers.

Figure 1.1 Map showing the sub-districts of Johannesburg metropolitan health district.



Key: 1 and 2 = sub district **A**; 3 and 4 = sub district **B**; 5 = sub district **C**; 6 and 10 = Sub district **D**; 7 = sub district **E**; 8 and 9 = sub district **F**; 11 = sub district **G**

3.3 Study population

The study population included all mothers together with their new-born babies delivered at term at SRH between 1 January 2013 and 31 December 2014.

3.4 Study sample

The minimum sample size (n) required was determined by the formula.[45]

$n= [(2pq) (Z\alpha+Z\beta)]/ (p_1-p_2)^2$

Where Zα is the normal deviate corresponding to the level of the significance, here 1.96 (95% confidence).

Zβ is the normal deviate corresponding to two tailed probability, 1.65(80% power). Odds ratio, OR equals 2.

P_1 = proportion of exposure in cases.

P_2 = proportion of exposure in control.

$q_1 = 1-P_1$ and $q_2 = 1-P_2$.

$P_1 = OR (P_2) / P_2 (OR-1) +1= 45.1\%$.

There were various exposures of interest with the prevalence of exposures ranging from 0.1% (multiple pregnancies) to 29.1% (HIV).[46] HIV had the highest risk prevalence; it was therefore used in the calculation of sample size to generate an adequate sample size.

$Z\alpha = 1.96$ $Z\beta = 1.65$ $P_1 = 45.1$

$P_2 = 29.1$ $q1 = 54.9$ $q2 = 70.9$

Hence, $n = [(2pq) (Z\alpha+Z\beta)] / (p1-p_2)^2$.

=184 cases and 184 controls.

However, efforts were made to enrol all eligible mother-baby pairs encountered during the study period. A total of 480 participants were enrolled for the study to increase the power of the study and to mitigate against the effects of files with incomplete data.

3.5 Inclusion criteria

1. All mothers who delivered a singleton live term baby, weighing less than 2500 grams at birth at SRH between 1 January 2013 and 31 December 2014 (case).

2. All mothers who delivered a singleton live term baby, weighing 2500 grams or more at birth at SRH between 1 January 2013 and 31 December 2014 (control).

3. All mothers whose duration of amenorrhoea was at least 37 completed weeks as calculated by the mother's sure last normal menstrual period (LNMP), earliest documented ultrasound report, symphysis-fundal height measurements or gestational age estimation by a paediatric doctor at birth.

4. All mothers who delivered by vaginal delivery assisted delivery or caesarian section.

3.6 Exclusion criteria

1 All mothers of babies with suspected or documented single gene defects, chromosomal abnormalities, dysmorphic features or congenital abnormality.

2 All mothers who delivered their babies before they at arrived at SRH.

3.7 Selection of study participants

3.7.1 Identification of cases

All deliveries that took place at SRH are recorded in the SRH birth register, this register is kept in the maternity ward of SRH. This register records the following information about mothers; names, age, hospital number and address. It also contains names of referring clinics, date of delivery, modes of deliveries, babies' weights, gestational age (term or preterm) and the sex of the babies. Cases were identified from this delivery register.

3.7.2 Selection of cases

The selection process was done month to month starting from 1 January 2013 and ending on 31 December 2014. The researcher searched the birth register looking for mothers who delivered a live term singleton LBW baby (pregnancy duration of at least 37 completed weeks with a birth weight of less than 2.5 kg). When such a mother was found on the birth register, a decision was made based on the inclusion criteria as to whether the mother-baby pair was eligible for inclusion in the study.

If the mother-baby pair was eligible for inclusion in the study, the hospital registration number, the age of mother and the sex of the baby were then obtained from the birth register. This information was then entered into the case/control registration form (Appendix 6 page number 68). All eligible cases identified were recorded on the case/control registration form and an individualised matching control(s) was looked for.

3.7.3 Matching of participants

Individualised one to one matching was done using the age of mothers and the sex of babies as matching variables. The matching of the age of mothers was done using an age class interval of five (16-20, 21-25, 26- 30 etc.). This age class interval of five is believed to be narrow enough for mothers within the same age class interval to have similar characteristics.[45]

3.7.4 Identification and selection of control

The researcher perused through the birth register for a mother who delivered a live term NBW baby (birth weight of 2.5 kilogrammes or more) on the same day as the birth of the case baby (i.e. both control and case mother delivered on the same day).

The researcher looked for a control (mother and her new-born baby) who met the matching criteria.

When such a mother-baby pair (control) was found on the birth register, the researcher checked whether the control met the inclusion criteria for the study. If the inclusion criteria were met, he recorded her details against the corresponding case recorded in the case/control registration form. When more than one matching control were identified on the same day for a particular case, the researcher chose the mother whose age is closest to the age of the case mother. Where the age of the probable control mothers are similarly close to the age of the case mother, the researcher assigned different numbers to the respective probable controls. Each number was then written in a small piece of paper, folded and placed in a small container. They were mixed together in this container and the researcher blindly picked one of the pieces of folded papers. This was to give each mother an equal chance of being picked. The mother-baby pair represented by the chosen number was then chosen as the matching control mother.

The process of case identification, case selection and matching with control described above was done for all days of the study period, 1 January 2013 to 31 December 2014. Attempts were made to match all cases on a particular day by looking for controls delivered on the same day because of possible seasonal variations in birth weight.[47] When a case and its matching control could not be selected on the same day, the following day(s) were checked for matching controls. Cases that could not be matched after going through the whole study period were excluded from the study.

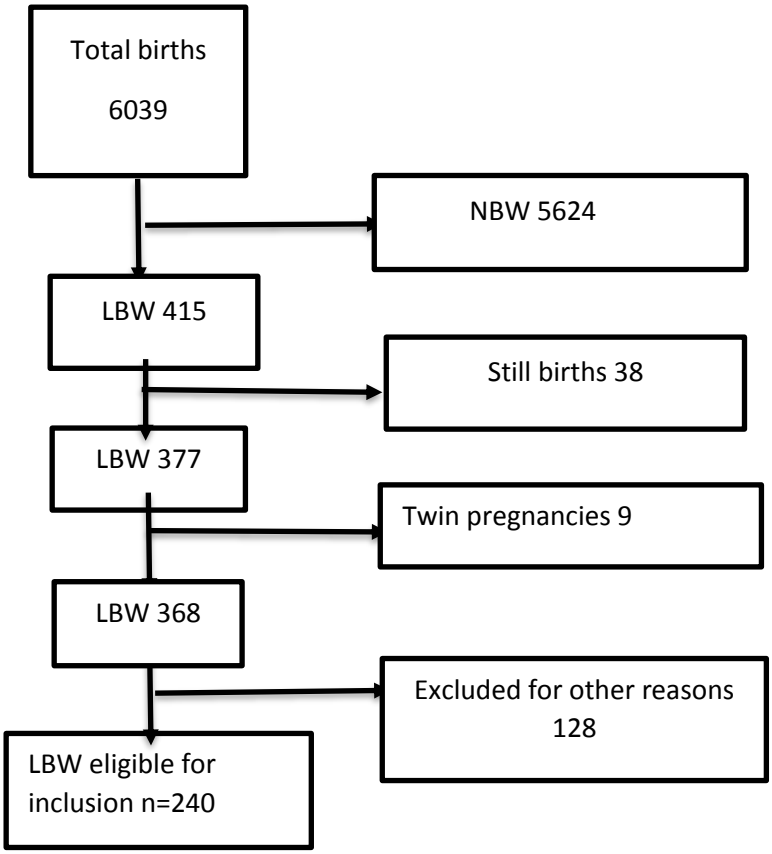


Figure 4.0 Flow chart showing the case selection process.

3.7.5 File retrieval

Files of mothers who delivered at SRH are kept at SRH except for those mothers who were transferred from SRH to other hospitals. The file numbers of the study participants (cases and their matched controls) were given to the clerical officer to retrieve the mothers' hospital record files. Once the files were collected from the clerk, the researcher re-checked the files for their eligibility for inclusion in the study. When either a case or a control file could not be found, attempts were made to re-match the available file using the same matching procedure described above. Available files that could not be re-matched were excluded from the study.

3.8 Data collection

The researcher extracted information from files retrieved from the records department. Socio-demographic and clinical characteristics of mother-baby pairs were recorded on the information extraction form (Appendix 3 page 59-62). The same study number was assigned to a pair of data extraction forms used to extract information from a particular case and its individually matched control. Each study number is linked to two hospital numbers; one for the case and the other for its matched control.

3.9 Measuring tool

The researcher developed a three-page information extraction form by considering the reported maternal risk factors for low birth weight in literature, the information available on the Gauteng provincial health antenatal card (Appendix 4 page number 63-64) and the maternal case record, MCR (Appendix 5 page number 65-67). This information extraction form had the following sections.

1. Demographic characteristics of the baby (question number 1 page 59); sex and weight of the baby. Recorded in grams to the nearest whole number.

2. Socio-demographic risk factors of mothers (question number 2 page 59); age, marital status, gravidity, parity, race, immigration status and employment status.

3. Maternal clinical risk factors (question number 3 pages 60-61); hypertensive disorders, HIV status, HIV positive on treatment, HIV positive on PMTCT, TB on treatment, TB completed treatment, ANC attendance, timing of ANC booking, number of ANC visits, haemoglobin level at first ANC visit, most recent haemoglobin level in third trimester and average weight gain per week after first trimester. Weight gain was recorded in kilogrammes to one decimal place.

4. Maternal behavioural risk factors (question number 4 page 61); smoking and alcohol consumption.

3.10 Data analysis

Information was transferred from the information extraction form onto a Microsoft excel spreadsheet. Data was exported into STATA 12 statistical software for data cleaning, coding and re-coding for statistical purposes. Data was analysed using STATA 12 statistical software with the help of statisticians. Descriptive analyses of categorical exposure variables were carried out and results presented as frequencies and percentages. The result of numerical variables were presented as means and standard deviations.

Inferential statistics executed included McNemar Chi-square test for binary categorical variables, paired t-test for continuous variable and logistic regressions analysis. The results of bivariate conditional logistic regression analysis were presented as an unadjusted odds ratio. Multivariate conditional logistic regression analysis (MLR) was carried out by the step-wise method. No imputation was done for missing values. Missing values were dealt with by the default way that STATA normally deals with missing values in logistic regression. The unknown category were already factored-in during the data analysis. Only variables with P values of less

than 0.1 in the bivariate conditional logistic regression analysis were included in the multivariate conditional logistic regression model. The results of multivariate conditional logistic regression were presented as an adjusted odds ratio. A P value <0.05 was considered significant.

For the purpose of analysis, some numerical variables; parity, the timing of ANC booking, average maternal weight gain per week after the first trimester of pregnancy and number of ANC attendance were transformed and re-coded as categorical variables. Haemoglobin level at first ANC visit and most recent haemoglobin level in the third trimester were re-coded into an ordinal variable; no anaemia, mild anaemia, moderate anaemia and severe anaemia.

3.11 Pilot

A pilot study was done after ethical approval was granted. Pilot study was conducted at SRH to check the adequacy of the case/control registration form and the data extraction form. This pilot study used ten matched participants who delivered at SRH in 2015. The case and control selection process, data collection and data analysis techniques of the original study were used on the pilot participants. This pilot study proved that a case-control study could be done without any deficit in the methodology and the data collection tool. The pilot files were not included in the analysis of the main study.

3.12 Ethical considerations

Ethical clearance for this study was granted by Human Research Ethics Committee of the University of the Witwatersrand, HREC (Appendix 1 page 57). Written permission to conduct the study was also granted by the Chief Executive Officer (CEO) of SRH (Appendix 2 page 58). Confidentiality of patients' information was ensured by not having patients' hospital numbers or their names on the information

extraction forms but the study numbers. This was a record review, a signed consent form from the participants of the study was not needed. By coming to use the health facilities, patients gave consent for their medical records to be used in research.

3.13 Funding

This study was fully funded by the researcher.

CHAPTER 4

RESULTS

4.1 Study population

4.1.1 Sample selection

A total of 6039 babies were delivered during the study period, 415 LBW babies, 5624 NBW, 64 stillbirths (38 LBW stillbirths, 26 NBW stillbirths) and 9 twin pregnancies. This equates to a proportion of LBW (term SGA) of 6.9% over the study period. After applying inclusion and exclusion criteria, 240 cases were matched with 240 controls. Figure 4.0 gives the flow chart of the case selection process.

4.2 Characteristics of the study participants

4.2.1 Distribution of study participants by matching variables

There were 480 study participants, 240 in each group, case and control (Table 4.1). The age ranges were 16 to 43 and 16 to 44 years among control and case groups respectively. Fifty-three percent of the participants were in the age group 21-30 years. There were 49% new-born female babies and 51% new-born male babies.

Table 4.1. Distribution of cases and controls as per matched variables

VARIABLES	Birth weight <2500g (n=240)			Birth weight ≥2500g (n=240)		
	N	%	Mean ± SD	N	%	Mean ± SD
AGE OFMOTHERS (YEARS)			27.8± 6.2			27.6 ± 5.9
16-20	34	14.2		34	14.2	
21-25	61	25.4		61	25.4	
26-30	67	27.9		67	27.9	
31-35	49	20.4		49	20.4	
36-40	24	10.0		24	10.0	
41-45	5	2.1		5	2.1	
Total	240	100		240	100	
SEX OF BABY	N	%		N	%	
Female	117	48.8		117	48.8	
Male	123	51.3		123	51.3	
Total	240	100		240	100	

4.2.2. Maternal socio-demographic and behavioural characteristics

Most of the participants were black single unemployed mothers (Table 4.2). The percentage of LBW among single and married mothers was (181/334; 54%) vs (53/140; 37%)} respectively. About 36% (177/480) of study participants were immigrant mothers and they gave birth to 28% (67/240) of babies with LBW. The percentage of LBW baby among nulliparous and multiparous women were {(87/161; 54%) and (153/319; 48%)} respectively.

The rate of smoking was 19% and 4% among cases and control groups respectively. Similarly, the alcohol consumption rate was 10% and 2% amongst case and control groups respectively.

Table 4.2 Socio-demographic and behavioural characteristics of mothers

VARIABLE NAMES	Birth weight <2500g (case, n=240)			Birth weight ≥2500g (control, n=240)		
	N	%	Mean ± SD	N	%	Mean ± SD
RACE						
Black	208	86.7		215	89.7	
Coloured	19	7.9		11	4.6	
White	13	5.4		10	4.2	
Indian	0	0		2	0.8	
Chinese	0	0		2	0.8	
MARITAL STATUS						
Single	181	75.4		153	63.8	
Married	53	22.1		87	36.3	
Divorced	3	1.3		0	0	
EMPLOYMENT STATUS						
Unemployed	164	68.3		157	65.4	
Employed	65	27.1		76	31.7	
Student	8	3.3		5	2.1	
IMMIGRATION STATUS						
Citizen	159	66.3		123	51.3	
Immigrant	67	27.9		110	45.8	
PARITY						
Nulliparous	87	36.3		74	30.9	
1-3	146	60.8		161	67.1	
≥4	7	2.9		5	2.1	

Table 4.2 contd. Socio-demographic and behavioural characteristics of mothers

	Birth weight <2500g (case, n=240)			Birth weight ≥2500g (control, n=240)		
	N	%	Mean ± SD	N	%	Mean ± SD
SMOKING (cigarette)						
Does not smoke	169	70.4		220	91.7	
Smokes	46	19.2		10	4.2	
ALCOHOL						
Does not drink alcohol	190	79.2		225	93.8	
Drinks alcohol	24	10.0		5	2.1	

4.2.3 Distribution of maternal clinical factors between groups

In both groups, most (64%) of the ANC bookings occurred in the second trimester of pregnancy (Table 4.3). Most of the mothers attended ANC clinic three to four times and only a small proportion attended more than six times. In each category of number of ANC clinic attendance, there were more control than cases that attended ANC except for the 1-2 number of ANC clinic attendances. Among mothers who were anaemic at booking, delivery of LBW baby was equally common among cases and control groups (26%). Among mothers who were not anaemic at booking, LBW delivery was less common compared to NBW baby.

Most recent haemoglobin level; there were 83 and 54 anaemic mothers amongst cases and control groups respectively. Mothers with a hypertensive disorder during pregnancy gave birth to four times more LBW babies than NBW babies. HIV status had a similar distribution between case and control groups. Almost half of the participants (227/480; 47%) had inadequate average maternal weight gain per week after the first trimester. History of a prior miscarriage was one and a half times more common in the case group compared to the control group { (37/240; 15%) vs (24/240; 10%)}.

Table 4.3 Distribution of maternal clinical factors

VARIABLES	Birth weight <2500g (case, n=240)			Birth weight ≥2500g (control, n=240)		
	N	%	Mean ± SD	N	%	Mean ± SD
TIMING OF ANC BOOKING			20.8 ±9.7			23.4 ±5.6
Unbooked	31	12.9		2	0.8	
1st trimester	11	4.6		4	1.7	
2nd trimester	136	56.7		172	71.7	
3rd trimester	62	25.8		62	25.8	
NUMBER OF ANC VISITS			2.6±0.1			3.5±0.1
Unbooked	31	13.0		2	0.8	
1-2	87	36.3		59	24.6	
3-4	97	40.4		125	52.1	
5-6	22	9.2		42	17.5	
>6	3	1.3		12	5.0	
HAEMOGLOBIN LEVEL AT FIRST ANC VISIT(g/dl)			11.9 ±2.0			12.1 ±1.6
No anaemia (11 or more)	145	60.4		176	73.3	
Mild anaemia (10 - < 11)	39	16.3		35	14.6	
Moderate anaemia (7- < 10)	20	8.3		26	10.8	
Severe anaemia (< 7)	3	1.3		1	0.4	

Table 4.3 contd. Distribution of maternal clinical factors

VARIABLES	Birth weight <2500g (case, n=240)			Birth weight ≥2500g (control, n=240)		
	N	%	Mean ± SD	N	%	Mean ± SD
MOST RECENT HAEMOGLOBIN LEVEL IN THIRD TRIMESTER g/dl)			11.7±1.7			12.1±1.5
No anaemia (11 or more)	157	65.4		186	77.5	
Mild anaemia (10 - < 11)	57	23.8		34	14.2	
Moderate anaemia (7- < 10)	24	10.0		20	8.3	
Severe anaemia (< 7)	2	0.8		0	0	
HYPERTENSIVE DISORDERS OF PREGNANCY						
No hypertension in pregnancy	209	87.1		234	97.5	
Hypertension in pregnancy	20	8.3		5	2.1	
HIV STATUS						
HIV negative	181	75.4		189	78.8	
HIV positive on treatment						
HIV positive on HAART	53	22.1		49	20.4	
HIV positive on PMTCT	1	0.4		2	0.8	
AVERAGE MATERNAL WEIGHT GAIN PER WEEK AFTER 1ST TRIMESTER (kg/week)			0.4±0.2			0.5±0.3
Adequate weight gain (≥0.5)	21	8.8		52	21.7	
Poor weight gain (<0.5)	111	46.3		116	48.3	
MISCARRIAGE						
Had miscarriage	37	15.4		24	10.0	
No miscarriage	203	84.6		216	90.0	

4.3 Inferential statistics

4.3.1 Comparison of maternal risk factors between cases and control

There was no significant difference between maternal age, parity and haemoglobin level at fist ANC clinic visit between case and control groups (Table 4.4). The most recent maternal haemoglobin level in the third trimester, average maternal weight gain per week after the first trimester, the number of ANC clinic visits and weight of babies were significantly different between the two groups. The most recent maternal haemoglobin level in the third trimester was lower than the maternal haemoglobin level at first ANC clinic visit in the case group (p= 0.016). In the control group, there was no significant difference (p= 0.993) between the two maternal haemoglobin measurements (Table 4.5). All categorical exposure variables were shown to be associated with LBW except for employment status and parity (Table 4.6).

Table 4.4. Paired t-test for numerical variables

Variables	Birth weight <2500g (case, n=240)		Birth weight ≥2500g (control, n=240)		**P value**
	N	Mean ± SD	N	Mean ± SD	
Parity	240	1.1±1.1	240	1.1±1.0	0.583
Maternal haemoglobin level at first ANC visit (g/dl)	207	11.9±2.0	207	12.1±1.9	0.327
Most recent maternal haemoglobin level in third trimester (g/dl)	240	11.7±1.7	240	12.1±1.5	0.001
Average maternal weight gain per week after 1st trimester (kg/week)	132	0.4±0.2	132	0.5±0.3	0.005
Number of ANC visits	240	2.6±0.1	240	3.5±0.1	<0.001

Table 4.5. The difference between first and third trimester haemoglobin levels in cases and in controls.

Variables	Mean difference in maternal haemoglobin levels {(Hb level at first ANC visit – Hb level in the third trimester) g/dl}	Confidence interval (95% CI)	P value
Haemoglobin (LBW)	0.306	0.057- 0.556	0.016
Haemoglobin (NBW)	0.001	-0.264- 0.261	0.993

Table 4.6. McNemar Chi-square test for binary categorical variables and LBW

Variables	Chi-square	P value
Race	135.58	<0.001
Immigration	8.93	0.002
Smoking	141.23	<0.001
Alcohol	175.51	<0.001
HIV status	72.84	<0.001
Hypertensive disorders	194.70	<0.001
Miscarriage	126.64	<0.001
ANC attendance	159.29	<0.001
Marital status	13.57	0.001
Employment status	1.70	0.427
Parity	2.12	0.347

4.3.1. Regression analysis

In the bivariate logistic regression, the following maternal factors decreased the odds of delivering a LBW baby; being married, immigrants, having attended ANC clinic, and having a maternal haemoglobin level in the third trimester of 11g/dl or more. On the other hand, smoking, alcohol consumption, having hypertensive disorder during pregnancy and average maternal weight gain of less than 0.5kg/week all increased the odds of delivering a LBW baby (Table 4.7).

In the multivariate conditional logistic regression, having a recent maternal haemoglobin level in the third trimester of 11g/dl or more, having attended ANC clinic, having more than four ANC clinic visits and being an immigrant, all decreased the odds of delivering a LBW baby, while smoking increased the odds of delivering a LBW baby (Table 4.8).

Table 4.7 Bivariate conditional logistic regression analysis

Risk factors	Number of observations	Unadjusted odds ratio	95% Confidence interval	P value
Parity	480			
Nulliparous (referent)		1.00		
1-3		0.72	0.46-1.12	0.145
4 or more		1.04	0.31-3.50	0.954
Black race (Referent: race other than black)	480	0.77	0.45-1.32	0.347
Married (referent: single)	474	0.60	0.41- 0.88	0.009
Employment status	475			
Unemployed (referent)		1.00		
Employed		0.81	0.53-1.22	0.309
Student		1.97	0.59-6.53	0.270
Immigration status	438			
Non-immigrant (referent)		1.00		
Immigrant		0.44	0.30-0.68	<0.001
Smoking during pregnancy	410	6.50	2.75- 15.35	<0.001
Alcohol consumption during pregnancy	408	5.25	1.80- 15.29	0.002
Miscarriage (referent: had no miscarriage)	480	1.62	0.94-2.79	0.083
HIV positive (referent: HIV negative)	470	1.09	0.68- 1.74	0.718
ANC attendance (referent: unbooked)	480	0.06	0.02- 0.27	<0.001
Timing of ANC booking	480			
Unbooked (referent)	-	1.00	-	-
1st trimester		0.18	0.03-1.12	0.066
2nd trimester		0.06	0.02-.027	<0.001
3rd trimester		0.07	0.02-0.32	<0.001

Table 4.7 Contd. Bivariate conditional logistic regression analysis

Risk factor	Number of observation	Unadjusted odds ratio	95% confidence interval	P value
Number of ANC visits	480			
Unbooked (referent)		1.00		
1-2		0.11	0.03-0.49	0.004
3-4		0.07	0.02-0.29	<0.001
5-6		0.05	0.01- 0.22	<0.001
More than 6		0.02	<0.01-0.15	<0.001
Haemoglobin level at first ANC visit (g/dl)	410			
Hb <11 (referent)	-	1.00		
Hb ≥ 11		0.77	0.49-1.18	0.229
Most recent haemoglobin level in third trimester (g/dl)	480			
Hb <11 (referent)	-	1.00		
Hb ≥11		0.55	0.36-0.83	0.004
Hypertensive disorders (referent: no hypertensive disorders)	456	4.75	1.62- 13.96	0.005
Average maternal weight gain per week after 1st trimester (referent: weight ≥ 0.5kg)	182	3.00	1.28-7.05	0.012

Table 4.8. Multivariate conditional logistic regression analysis

Variables	Adjusted Odds Ratio	95% Confidence interval	P value
Most recent haemoglobin level in third trimester (g/dl)			
Hb <11.0 (referent)	-		
Hb 11.0 or more	0.540	0.293- 0.996	0.048
Timing of ANC booking			
1st trimester (referent)	-	-	
Unbooked	0.189	0.015-2.274	0.190
2nd trimester	0.114	0.023-0.565	0.008
3rd trimester	0.073	0.012-0.411	0.003
Number of ANC visits			
1-2 (referent)	-	-	
Unbooked (omitted)			
3 -4	0.593	0.278-1.264	0.176
More than 4	0.359	0.170-0.755	0.007
Immigrant	0.457	0.247-0.848	0.013
Smokes during pregnancy	8.686	2.660-28.351	<0.001
Hypertensive disorder in pregnancy present.	2.886	0.751-11.090	0.123
Consumed alcohol during pregnancy	2.406	0.659-8.783	0.184
Married	0.712	0.413-1.228	0.222

CHAPTER 5

DISCUSSION

In this chapter, the results of this study are compared with those of similar studies in the context of the objectives of this study. This chapter was discussed with the followings as subheadings: methodology, the incidence of LBW, association between independent variables and LBW and regression analysis.

5.1 Methodology

An ideal study design to answer this research question would be a prospective cohort study, but it would require an enormous amount of time to follow up the participants. Due to time and other resource constraints, the researcher could not embark on a prospective cohort study. The retrospective nature of this study meant that results of this study depend on the quality of the data recorded in the files and how accurate the recorded values represent the true situations.

5.2 Incidence of LBW

The proportion of LBW (term SGA) in this study was 6.9%, it is lower than the rates reported for SGA at term in Brazil and Tanzania which were 13.1% and 15.8% respectively.[42] This relatively small proportion of term SGA reported in this study is similar to the reported prevalence in high-income countries. The results of this study should be carefully interpreted. This study was conducted at a level one hospital, where high-risk patients are expected to be identified during antenatal clinic visits and promptly referred to a higher level of care for delivery. This is recommended practice according the Basic Antenatal Care Guideline (BANC) and if followed strictly should keep the number of LBW deliveries low at centres like SRH but higher at tertiary centres. Higher levels of care tend to have a higher LBW incidence than national averages.[1]

5.3 Association between variables and Regression analysis

5.3.1 Socio-demographic and behavioural risk factors

5.3.1.1 Age of mothers

The overall age range of the mothers was 16- 43 years and the maternal modal age group was 26-30 years. Pedro reported 10-19years and >40 years as lowest and highest age class intervals respectively in a study in Brazil.[48] The modal age group in most studies depends on the age class interval used, but they generally tend to fall below the third-decade of life.[49]

Matched case-control studies by design should have a similar mean maternal age between case and control groups as was seen in this study. However, the mean maternal age in an unmatched case-control study may also be similar between case and control groups as reported in a study in Nepal.[50] This observation suggests that the distribution of maternal ages was uniform in that study. Teenage mothers constituted 14% of the total number of mothers in this study, this is lower than 19% reported in the Nepal study cited above. The age of mother was not investigated as a risk factor for LBW in this study because it was a matching variable. In studies where the age of mother was investigated as a risk factor for low birth weight, the results vary remarkably depending on the referent age class interval.[51] The other matching variable in this study, sex of babies, was not investigated for the same reason.

5.3.1.2 Race

The majority of the study participants were black mothers (88%) and the other races constituted about 11% of study participants. This is an expected finding given the predominance of black race in the study community. Studies of this nature tend to reflect the socio-economic and racial distribution of their study populations.[45] This

finding could also be due to a racial selection bias common with studies conducted in most public hospitals in South Africa.

Race in this study, was associated with LBW, p <0.001. However, in the bivariate logistic regression, with race other than black as the referent group, race was not a significant risk factor for low birth weight, OR=0.77, P=0.347. A similar finding was reported in a study in Brazil by Zambonato,[24] using the white race as the referent group. The findings of this study are contrary to the finding by Tierney-Gumer in the USA. He found that African-Americans were seven times more likely to give birth to LBW babies compared to European-Americans or Hispanics.[35] Thompson also reported that blacks and race other than white are twice and 1.3 times more likely to give birth to LBW babies compared to whites. [18] Several studies reported that African-Americans, Indians and Asians have higher odds of LBW compared to whites.

The inability to show race as a risk factor for LBW in this study may be due to a relatively small representation of races other than black, thus reducing the power of the study in this regard. It is difficult to investigate the effect of race on LBW because of the differences in other confounding factors such as, socio-economic status and nutrition.[40]

5.3.2.3 Marital status

In this study, the majority of the mothers were single mothers (69.6%). This finding contrasts the findings of similar studies done at Bale hospital in South-East Ethiopia and Maharashtra with 92% and more than 50% respectively of study participants being married mothers.[45, 52] The finding of a high percentage of single mothers in the current study could be a reflection of the social circumstances in the study population and possibly the country as a whole.[53] Marital status was positively associated with LBW, p= 0.001.

Being married was a significant risk factor for LBW in the bivariate analysis (OR=0.6, p= 0.009) but not in the multivariate regression analysis. This finding was supported by Thompson who reported that being single is a risk factor for LBW.[18] Contrary to the above findings, Habtamu reported that marital status was not significantly associated with LBW, OR=1.8, P= 0.131.[52] The reported observation in the Ethiopian study by Habtamu, could be due to the fact that 89.9 % of cases and 94% of controls were married. This low proportion of mothers in the other marital status categories could reduce the power of the study to detect a difference in this respect. Generally data on marital status and LBW is conflicting. It is reported that single and cohabiting women have increased odds of term low birth weight even after confounders were adjusted for.

5.3.2.3 Employment

The proportion of unemployed mothers in this study was (67%) this was significantly higher than the maternal unemployment rate of 47% reported in a similar study by Batist in Cape Town in 2003.[5] This higher unemployment rate in this study probably reflects the prevailing economic climate in South Africa at the time of this study. It could also be due to the fact that SRH is located in an area with a lot of immigrant mothers, the majorities of whom may not be employed. Similar observations of high unemployment rates were noted in studies in Karachi,[4] Northwest Ethiopia[1] and the Bale studies.[52] Employment status was not associated with LBW, P=0.427.

In this study, being employed or being a student was not a significant risk factor for LBW, P> 0.05. Unlike the findings of this study, Anaelina found that being a housewife was a risk factor for low birth weight compared to other occupations.[16] Habtamu also reported that farmers, merchants or daily labourers were less likely to deliver a LBW baby while being a housewife increased the risk of delivering LBW.[52]

5.3.2.4 Immigration

South Africans nationals were the majority of the study participants (59%), this was expected because the study was conducted in South Africa. Similar observations were noted in different studies conducted in various part of the world.[36] Immigration status was associated with LBW p=0.002.

In this study, immigrant mothers were less likely to deliver LBW babies (OR= 0.44, p <0.001) compared to non- immigrant mothers. This result is corroborated by a USA study which reported that foreigners were less likely to deliver LBW babies.[18] A Belgian study also reported that all nationalities other than Belgians were less likely deliver LBW baby compared to Belgians, except sub-Sahara Africa. Sub-Sahara African mothers had a higher risk of delivering LBW baby than Belgians, but after adjusting for employment status, the likelihood of delivering LBW was similar between sub-Saharan African and Belgians mothers.[18] South Rand hospital catchment areas have a sizeable number of immigrants from the Democratic Republic of Congo, Nigeria, and Ethiopia, these immigrants may have socio-economics condition that may be more favourable than the average South African user of the hospital.

5.3.2.5 Parity

About one-third of the study participants were nulliparous, 36% and 31% of these mothers were in the case and control group respectively. A similar result was reported by Pedro in Brazil,[48] where 35% and 31% of nulliparous mothers were among case and control groups respectively. Habtamu also reported that about one-third of the participants were nulliparous of which 43% and 28% were in case and control groups respectively.[52] The average parity in this study was one and there was no significant difference between the average parities of the two groups, paired t-test, p=0.583. Parity was not associated with LBW, McNemar Chi-square test, p=0.347.

Using nulliparous women as the referent class, multi-parity was not a risk factor LBW, p >0.05. In the literature, there have been wide variations in the conclusions reached on the influence of parity on LBW. Some studies supported the findings of this study, Sachin[54] and Bolajoko.[30] Studies with contrary findings include a report by Berihum in Ethiopia, Pedro in Brazil and Miguel in Spain.[55] This variation in findings from different studies was probably due to the fact it was difficult to control for parity and the fact that parity relates to other maternal factors, such as age and socio-economic status.

5.3.2.6 Smoking (cigarette)

In this study, 19% of case mothers and 4% of the control mothers smoked. The reported percentages of maternal smoking during pregnancy varied widely from one part of the world to another. It could be as high as 62% and 34% among cases and control groups respectively (as reported in a Cape Town study),[5] or as low as 15% and 12% of cases and control respectively, in a study in Nepal.[50] In some studies, the percentage of mothers who smoked during pregnancy is several times higher (about two to ten times) among case mothers than control mothers.[54] A study conducted at the University of Granada hospital showed an almost equal percentage of mothers who smokes cigarette during pregnancy between case and control mothers.[55] This observation of similar exposure percentage between the two groups in the Spanish study may be due to a higher prevalence of smoking in high-income nations. Smoking is positively associated with term LBW, P <0.001.

In this study, mothers who smoke during pregnancy were six and a half times more likely to deliver a LBW neonate compared to non-smokers, (OR=6.5, p<0.001). This finding is supported by studies in Brazil.[48] In one of the studies, it was reported that smoking beyond fourth months of pregnancy, irrespective of the number of cigarettes smoked per day increases the likelihood of delivering a LBW baby compared to mothers who never smoked (OR=1.53, CI= 1.38-1.68). Smoking up to the fourth month is not significantly associated with LBW (OR=0.98.CI= 0.64-1.48).

There is a consensus on the adverse effect of maternal smoking on birth weight. Studies have also shown a dose-dependent and causative relationship with LBW.[40] Evidence supports the fact that mothers who stopped smoking by 15 weeks of pregnancy had a rate of LBW similar to mothers who do not smoke.

5.3.2.7 Alcohol

In this study, 10% and 2% of mothers who reported that they consumed alcohol during pregnancy were among case and control groups respectively. The Cape Town study conducted at Wine land /West Coast region reported a much higher alcohol consumption rate among cases (55%) than what was observed in this study.[5] Sudesh et al, in contrast to findings of current study, reported alcohol intake during pregnancy to be very low and that the percentage of mothers who consumed alcohol during pregnancy were more in the control group than in the case group (1.3% control versus 0.6% case). Gail found an almost equal percentage of mothers used alcohol or other drugs during pregnancy (8.6%, case vs 9.8%, control) in a study at University of Pennsylvania.[28] In the current study, maternal alcohol consumption during pregnancy was positively associated with LBW, $p < 0.001$.

Mothers who consumed alcohol during pregnancy were five times more likely to deliver a LBW baby compared to mothers who did not (OR= 5.25, p= 0.002), in the bivariate regression analysis. The P value was not significant in the multivariate regression analysis. Lindsay reported that alcohol consumption during pregnancy increases the likelihood of delivering a LBW baby. [18]Another local study in the Eastern Cape also supported the finding by Lindsay.[14] An Italian study also reported that maternal alcohol consumption of three or more drinks daily at any trimester increase the odds of delivering SGA threefold and this effect remained even after confounders were adjusted for.[40] The inability of the current study to show alcohol as a significant risk factor for low birth weight was probably due to the small percentage of participants who reported alcohol intake during pregnancy. It was not possible to

quantify alcohol consumption during pregnancy in this study because of the study design.

5.3.3 Maternal clinical risk factors

5.3.3.1 Timing of ANC booking

Most of the mothers booked for ANC in the second trimester (64%) and the least number of bookings was in the first trimester (3%). Most studies did not investigate the timing of ANC bookings as a risk factor for low birth weight, they used the number of ANC visits as a proxy measure for the timing of an ANC booking. However, a study at Bale hospital in South-East Ethiopia reported a finding similar to this study's in the distribution of timing of ANC booking.[52] Almost 14% percent of mothers were unbooked in our study against 17% unbooked in the Bale zone study.[52] In this study, the mean gestational ages at ANC bookings were 21 and 23 weeks for case and control groups respectively. There was no significant difference between the mean gestational ages at ANC booking between the two groups. These mean gestational ages during ANC bookings were similar to the mean gestational ages at ANC booking (22 weeks) reported in a study in Cape the Winelands area.

Using unbooked mothers as the referent class, mothers who booked in second (OR= 0.06, P <0.01) or third trimester (OR= 0.07, P <0.01) were less likely to deliver a LBW baby compared to unbooked mothers. Booking in the first trimester does not appear to protect against LBW. This observation may be due to a relatively small number of mothers who booked in the first trimester (6%), compared to 64% and 25% in second and third trimester respectively. Similarly, in the multivariate logistic regression, using booking in the first trimester as the referent class, second trimester and third trimester booking were protective while the P value for unbooked mothers was not significant.

5.3.3.2 Number of ANC attendance

Average number of ANC visits was more than two among case whereas control mothers had more than three ANC visits. A similar observation was reported by Pedro and Sudesh.[48] There was a significant difference between the average number of ANC visits between the two groups, paired t-test, p <0.001.

In this study, mothers who booked for ANC were less likely to deliver a LBW baby compared to unbooked mothers. This level of protection increased with increasing numbers of ANC visits {(1-2 visits, OR= 0.11, p =0.004) vs (3-4 visits, OR=0.07, p= <0.001)}. There is a wide variation in the reported influence of the number of ANC visits on LBW. Although most articles reported a significant association between the number of ANC visits and LBW, the direction of the association depended on the number of visits used as the referent value. Anaelena, using seven or more ANC visits as referent value, reported that less than six ANC visits increased the likelihood of delivering a LBW baby.[16] A study conducted in Eastern Nepal used the number of ANC visits of more than four as the referent class, it was reported that 1-2 and 3-4 visits were all protective.[50] Ganesh classified ANC visits into regular and irregular visits and reported that with regular visits as the base group, ANC visits were not significantly associated with LBW, AOR= 1.28, CI= 0.57-2.90, p=0.55.[53] It would be interesting to know the author's definition of regular and irregular ANC visits, unfortunately, this definition was not given in the article.

5.3.3.3 Maternal haemoglobin level

5.3.3.3.1 Haemoglobin level at first ANC visit

The mean haemoglobin levels at the first ANC booking were 11.9g/dl (case) and 12.1 g/dl (control) with no significant difference between the two means, paired t-test, P= 0.327. Amongst the case group, mean haemoglobin levels during the first ANC booking were more than the most recent haemoglobin level in the third trimester or in labour, 95% C.I= 0.057- 0.556, p= 0.016.

Using anaemia at first ANC booking as a referent class, a third trimester haemoglobin level of 11g/l or more does not protect against delivering a LBW baby (OR=0.77, p=0.229). This finding may be due to the fact that haemoglobin levels in the earlier part of a pregnancy are as important as haemoglobin levels in the latter part of a pregnancy. Most Authors did not report on haemoglobin levels at the first ANC visit, but during labour or in the third trimester. This makes it difficult to compare results from this study with those of others.

5.4.14 Haemoglobin level in the third trimester

The mean of the most recent haemoglobin level measured in the third trimester or in labour was 11.7g/dl (case) and 12.1 g/dl (control) with a significant difference between the two means, paired t-test, P= 0.001. Among the control group, there was no significant difference between mean haemoglobin level during ANC booking and the most recent haemoglobin level in the third trimester or in labour, 95% C.I= -0.264- 0.261, p= 0.993.

In this study, using haemoglobin levels of less than 11g/dl as a referent class, most recent haemoglobin level in the third trimester of 11g/dl or more had a protective effect on the likelihood of delivering a LBW baby in the bivariate analysis (OR= 0.55, p= 0.004). Similar result were obtained in the multivariate logistic models, OR= 0.54, P= 0.048.

Tunny, using a similar referent class to the one used in this study, reported that anaemia in pregnancy increased the odds of delivering a LBW baby.[56] This finding was also upheld by Erika in a multi-country survey.[57] Contrary to the findings of this study, Ravi reported that maternal anaemia is associated with LBW but it is not (< 12g/dl) a significant risk factor for LBW in the multivariate logistic regression, AOR= 1.27, 95% CI= 0.59-2.71, p= 0.534.[50] This finding may be related to the cut off value used for the definition of anaemia in Ravi's study.

5.3.3.4 Hypertensive disorders of pregnancy

Hypertensive disorders in pregnancy were observed in about 5% of the participants in this study, more were observed in the case than in the control groups. A similar finding was reported by Sachin,[54] but the proportion of mothers with hypertension during pregnancy was much higher in the study by Sachin than in this study (23% case and 9% control). This lower percentage of mothers with hypertensive disorders in the current study could be due to the fact that the study was conducted in a level one hospital which caters for low to moderate risk mothers, whereas the study by Sachin was conducted at medical colleges, a higher level of care that caters for high-risk obstetric patients. Hypertensive disorder of pregnancy was positively associated with LBW when analysed using the McNemar Chi-square test, P<0.001. Hypertensive disorder of pregnancy was not a significant risk factor for LBW in the MLR probably because of the small percentage of mothers with hypertensive disorder of pregnancy. Most studies report hypertensive disorder of pregnancy as a significant risk factor for LBW.[26]

5.3.3.5 HIV status of mothers

About 25% of the study participants had a positive HIV test and the proportion of HIV-positive mothers who delivered LBW was slightly higher than those who delivered NBW neonates (22% versus 20%). A similar study at a referral hospital in Tanzania reported 10.5% of mothers were HIV positive and 20% of them gave birth to LBW neonates,[11] this finding is similar to the current findings. HIV positive status was positively associated with LBW when analysed using the McNemar Chi-square test, P <0.001.

Maternal HIV positive status did not predict LBW (OR=1.09, p= 0.718), in the current study. A similar result was reported by Izunwa.[14] A meta-analysis of cohort studies on the association between maternal HIV infection and LBW refuted this claim.[58] The meta-analysis reported a significant association between LBW and

maternal HIV infection, with a pooled Odds Ratio of 1.65, 95% CI=1.49-1.63, P<0.001. The odds of delivering a LBW baby by an HIV positive mother was found to be slightly higher in low and middle-income countries than in high-income countries. And the use of antiretroviral drugs did not significantly change this association. The variation in the current studies results and the result of the meta-analysis, could be due to inadequate power in this study to detect a difference. Also, a study by James in rural KwaZulu-Natal in a non-randomised intervention study reported that maternal HIV-positive status is a significant risk factor for LBW.[37]

5.3.3.6 Average maternal weight gain per week after the first trimester

In this study, about 47% of participants had inadequate weight gain per week (<0.5kg per week) after the first trimester of pregnancy. The distribution of mothers with inadequate weight gain was almost equal between the two groups. Contrary to this study, most studies investigated one of; maternal pre-pregnancy weight, maternal weight gain over the entire duration of the pregnancy or basal metabolic rate. The researcher decided to investigate maternal weight gain per week in this study because this parameter is more likely to detect an inadequate weight gain during pregnancy earlier than the other weight-related parameters mentioned above.

In contrast to the current study, Miguel et al reported that weight gain in their study was lower among case than control group participants and that there was a significant difference in mean weight gain per week between the two groups (P< 0.001).[55] There was an almost equal number of mothers with inadequate weight gain per week in both groups in this study, probably due to a disproportionately higher number of missing values in the control group compared to the case group. Sachin reported that weight gain during pregnancy was lower in the case group compared to the control group.[54] There was a significant difference between the mean maternal weight gain per week between case (0.4kg/week) and control (0.5kg/week) groups (paired t-test, p= 0.005). The average maternal weight gain per week reported in this study was higher than that reported by Miguel (0.24kg/week in case versus 0.29kg/week in control). In this study, mothers with inadequate weight gain during pregnancy were more likely to

deliver a LBW baby (OR= 3.0, P= 0.012) than those with an adequate weight gain per week after the first trimester.

There is a paucity of research that reports maternal weight gain per week as a risk factor for LBW. Miguel reported that maternal weight gain per week is a significant risk factor for LBW.[55] It must be pointed out that the cut-off point for adequacy of maternal weight gain in the study by Miguel is unknown and the average maternal weight gain per week among control mothers was about 299g/week. This value is below the lower limit for adequate maternal weight gain per week by the WHO. A possible explanation for the low maternal weight gain per week in the study by Miguel was the fact that the study was conducted with mothers who lived in places that were of a high altitude and this may influence maternal weight gain because of tissue hypoxia.

5.3.3.7 Miscarriage

There were 15% and 10% of mothers with a prior history of a miscarriage in the case and control groups respectively. This finding was different to Ganesh's finding of an almost equal distribution of number of mothers with a prior miscarriage history between case and control (7.3% and 8.7%) groups, in a district hospital in Karnataka. [53]Miscarriage is negatively associated with LBW, McNemar Chi-square test, $P<0.001$.

A prior history of miscarriage did not predict LBW (OR 1.62, p=0.083), in this study. Similarly, Sudesh reported that a prior history of miscarriage was not significantly related to the delivery of a LBW baby.[49] This finding was refuted by Gopomang who reported that mothers with a history of miscarriage are 1.3 times more likely to deliver LBW babies than mothers with no prior miscarriage history.[31] The results of this study may be related to a relatively small number of mothers with a prior history of miscarriage. However, studies on effect of a prior history of miscarriage on birth weight have reported mixed findings. [40]

CHAPTER 6

CONCLUSIONS AND RECOMMENDATIONS

6.1 Conclusions

This study investigated maternal risk factors for low birth weight using a relatively strong methodology, matched case-control. This study has shown that haemoglobin levels of 11g/dl or more in the third trimester and more than four antenatal care attendance has a protective effect on the likelihood of delivering a LBW baby, while, smoking during pregnancy increases the likelihood of delivering a LBW baby by about eightfold. Being an immigrant mother reduces the odds of delivering a LBW baby in this community. Alcohol consumption during pregnancy, hypertensive disorders of pregnancy and being married did not have a significant effect on the likelihood of delivering a LBW baby, this may be related to the power of the study.

6.2 Recommendations

The risk factors for low birth weight are multiple. It is therefore important to have an integrated approach to addressing these risks. It is recommended that anaemia in pregnancy should be prevented and haemoglobin of eleven g/dl or more should be aimed for.

Booking in the first trimester should be encouraged and all pregnant women who present for booking should be seen on the same day and not told to come back at a later day. Intervention programmes such as smoking cessation have been shown to work and should be instituted to reduce maternal smoking during pregnancy.[58]

The National Maternity Guideline does not recommend maternal weight measurement during each ANC visit. However, American Congress of Obstetrician and Gynaecology committee recommend different pregnancy weight gain for different maternal BMI categories.[60] One can only know whether or not a mother is within or outside recommended pregnancy weight gain by serial maternal weight measurement during ANC visits. Evidence also showed that

inadequate maternal weight gain is associated with delivery of LBW baby. On this basis, the Department of Health should consider redesigning the maternal case record to have space to record maternal weight and to have a maternal weight chart on the MCR, similar to the symphysis-fundal height (SFH) chart. This chart should have drawn maternal weight graphs for 90^{th}, 50^{th}, and 10^{th} centiles to make it easy to identify abnormal maternal weight gain during pregnancy early. Failure to adequately prevent LBW now may worsen the disease burden of future generations.

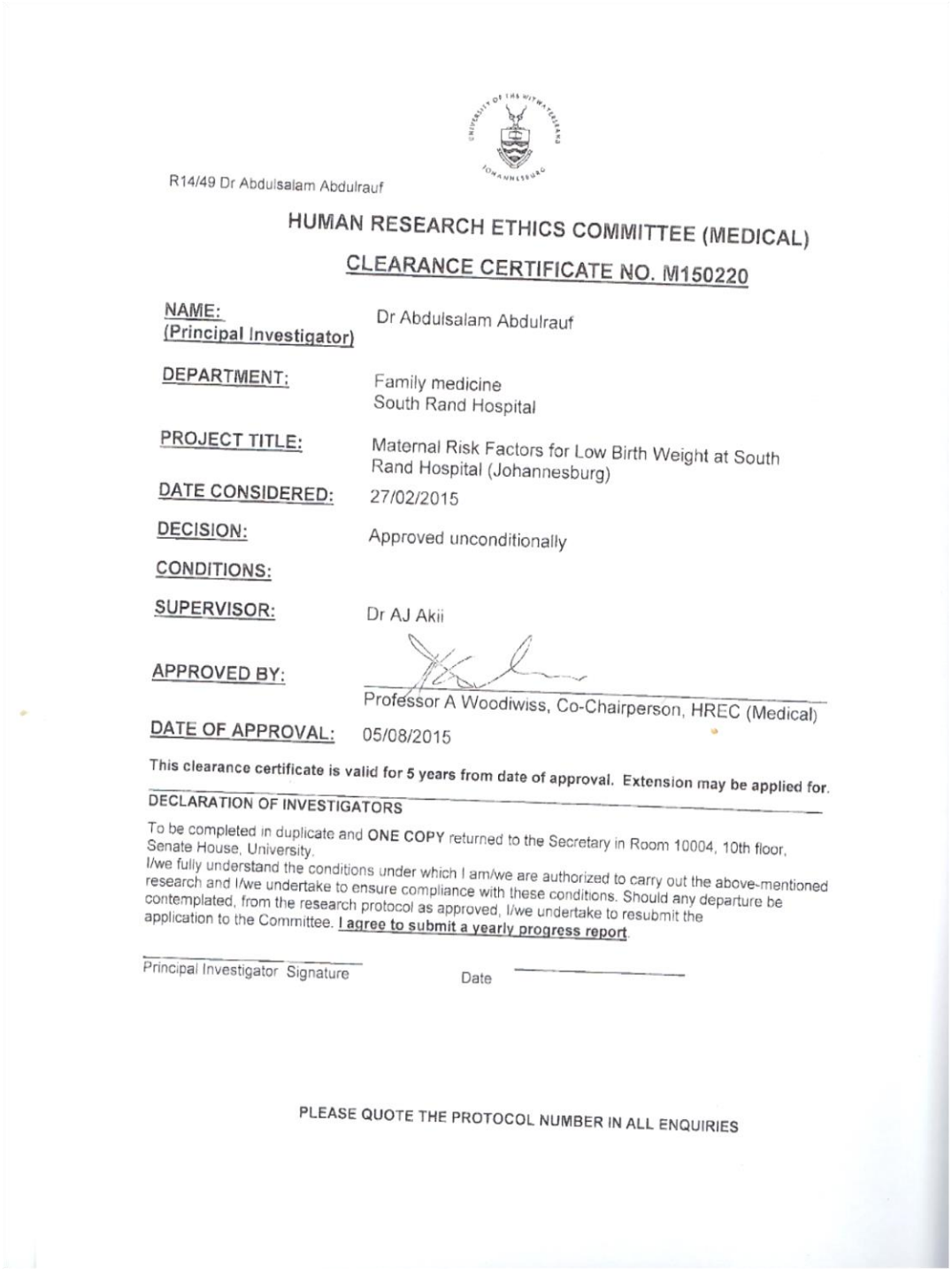
6.3 Limitations

This is a retrospective case-control study and all the limitations of case-control studies apply. The researcher relied on self-reporting of behavioural risk factors, a mother who drinks alcohol during pregnancy and is aware of the risk this act pose to the unborn foetus, may not disclose alcohol intake to clinicians. One is not able to quantify how much alcohol or cigarettes a mother drinks or smokes. Mothers who were cohabiting with their partners may report that they are single, but this situation may afford them advantages similar to what is enjoyed by married women. This study focused on mothers who delivered in a level one hospital, it does not include mothers who delivered in a higher level of care or at home. This will impact on the generalizability of our result.

There were a lot of missing values for the average maternal weight gain per week after the first trimester of pregnancy. A possible explanation could be the fact that the National Maternity Guideline did not recommend maternal weight measurement during follow up ANC visits.

Maternal age was recorded as in the file, mothers ages could have changed by the time they delivered depending on their date of birth and date of delivery. Age at delivery would have been more appropriate to use. Birth weight was taken as it was in the file, it is uncertain how often the weighing scales in the hospital are calibrated. Gestational ages were taken as recorded in the file. There is uncertainty with the accuracy of the gestational ages documented in the file, some term babies may not be truly term.

Appendix 1: Ethics Clearance certificate



R14/49 Dr Abdulsalam Abdulrauf

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M150220

NAME: (Principal Investigator)	Dr Abdulsalam Abdulrauf
DEPARTMENT:	Family medicine South Rand Hospital
PROJECT TITLE:	Maternal Risk Factors for Low Birth Weight at South Rand Hospital (Johannesburg)
DATE CONSIDERED:	27/02/2015
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Dr AJ Akii
APPROVED BY:	Professor A Woodiwiss, Co-Chairperson, HREC (Medical)
DATE OF APPROVAL:	05/08/2015

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Secretary in Room 10004, 10th floor, Senate House, University.

I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report**.

Principal Investigator Signature _____ Date _____

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

Appendix 2: Certificate of approval by the CEO of SRH

GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

SOUTH RAND HOSPITAL
ENQUIRIES
Office of the CEO
T: 011 681 2002
M: 0710872 6649
E: mokgadimaleka@gmail.com
20 April 2015

Dear sir

APPROVAL TO CONDUCT RETROSPECTIVE STUDY IN SUB-DISTRICT F OF JHB METRO HEALTH DISTRICT

This letter serves to confirm that you have been granted permission to conduct the above mentioned study at the South Rand Hospital.
I trust the results will assist us in the improvement of provision of service to our patient.

Kind Regards.

.....
Dr Maleka
Acting CEO: South Rand Hospital

Appendix 3: Information extraction form

Study number:

1. **Demographic characteristics of baby.**

	Male	Female
Sex of baby	☐	☐
Baby's weight (kg)	☐	

2. **Socio-demographic risk factors of mothers.**

Age (in years)	☐
Marital status (M,S,D,Wi)	☐
Gravidity	☐
Parity	☐
Race (W,C,B,In, Ch, O)	☐
Immigration status (I, N)	☐
Employment status(E,U)	☐

Site of ANC attendance:

3. Maternal clinical risk factors.

	YES	NO
Hypertensive disorders		
HIV status		
HIV positive on treatment		
HIV positive on PMTCT		
TB on treatment		
TB completed treatment		

	Yes	No
ANC attendance		

Timing of ANC booking

First trimester	
Second trimester	
Third trimester	

Number of ANC visit(s)

Visit 1	☐
Visit 2	☐
Visit 3	☐
Visit 4	☐
Visit 5	☐
Visit 6	☐
More than 6 visits	☐

Hemoglobin level at first ANC visit (g/dl):

Most recent hemoglobin level in third trimester (g/dl):
Average weekly weight gain in pregnancy (kg):

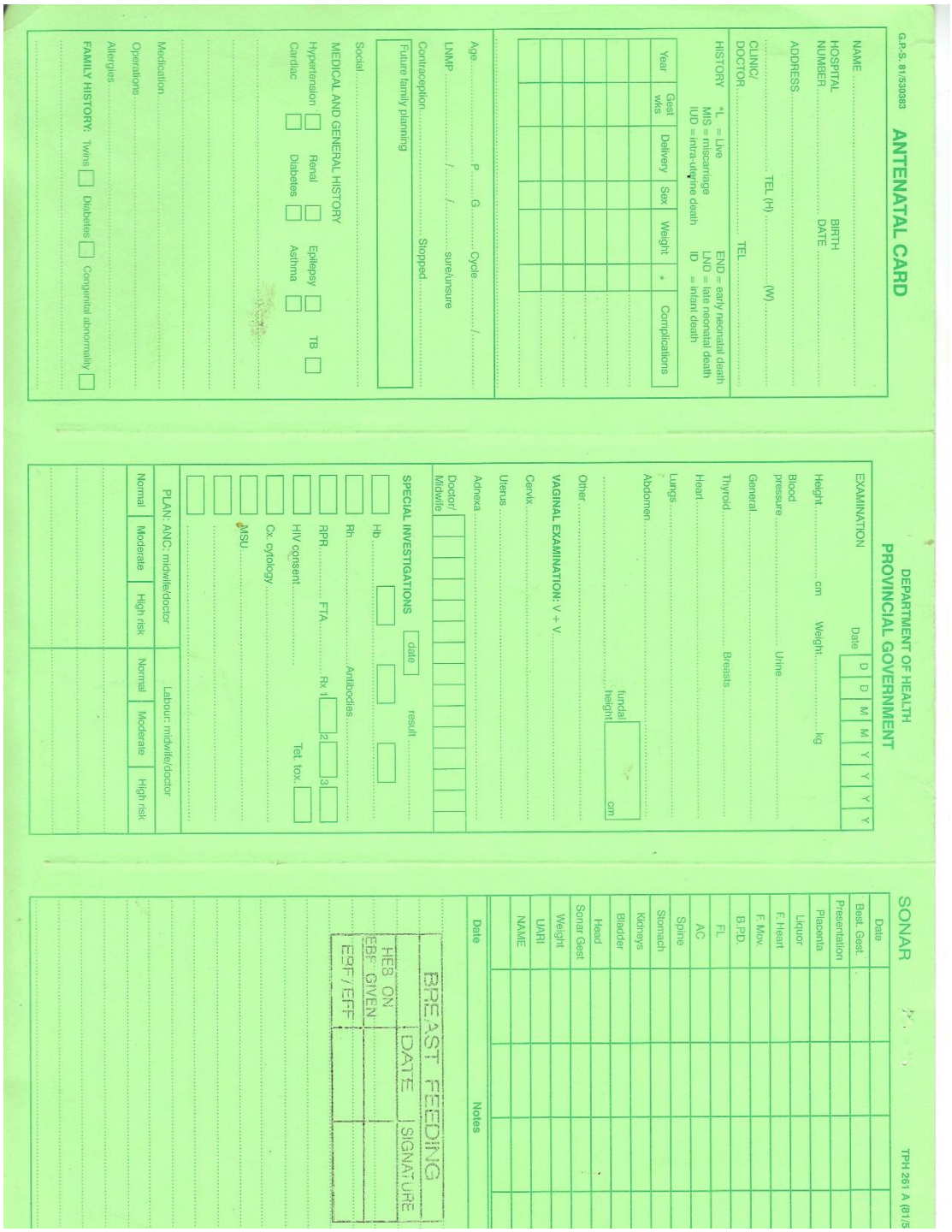
4. Maternal behavioral risk factors.

	Yes	No
Smoking	☐	☐
Alcohol	☐	☐

Key

B……Black
C……Colored
Ch……Chinese
D……Divorce
E……Employed
I……Immigrant
In……Indian
M……Married
N……Non- immigrant
S……Single
U……Unemployed
W……White
Wi……Widow

Appendix 4: Gauteng Provincial Government ANC card



DEPARTMENT OF HEALTH : PROVINCIAL ADMINISTRATION

ANTENATAL CARD

SIGNATURE:

DATE:

GESTATION 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43

GESTATION EST. BY

EDD

Dates

SF

Sonar

Best est.

DATE:

⊙=SF - measurement

X = weight

KG 30 25 20 15 10 5

45 cm 40 35

PRESENTING PART

HEAD ABOVE PELVIS(fifths)

GESTATION 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43

WEIGHT kg

BLOOD PRESSURE Syst. Diast

EDEMA

URINE P S P S

Fetal movements (First felt)

PROBLEM LIST

DATE

1

2

3

4

5

DATE NOTES (only essential facts)

SOUTH RAND HOSPITAL

ANTENATAL CLINIC

DATE SIGNA

Pre-Test information

Test and result today

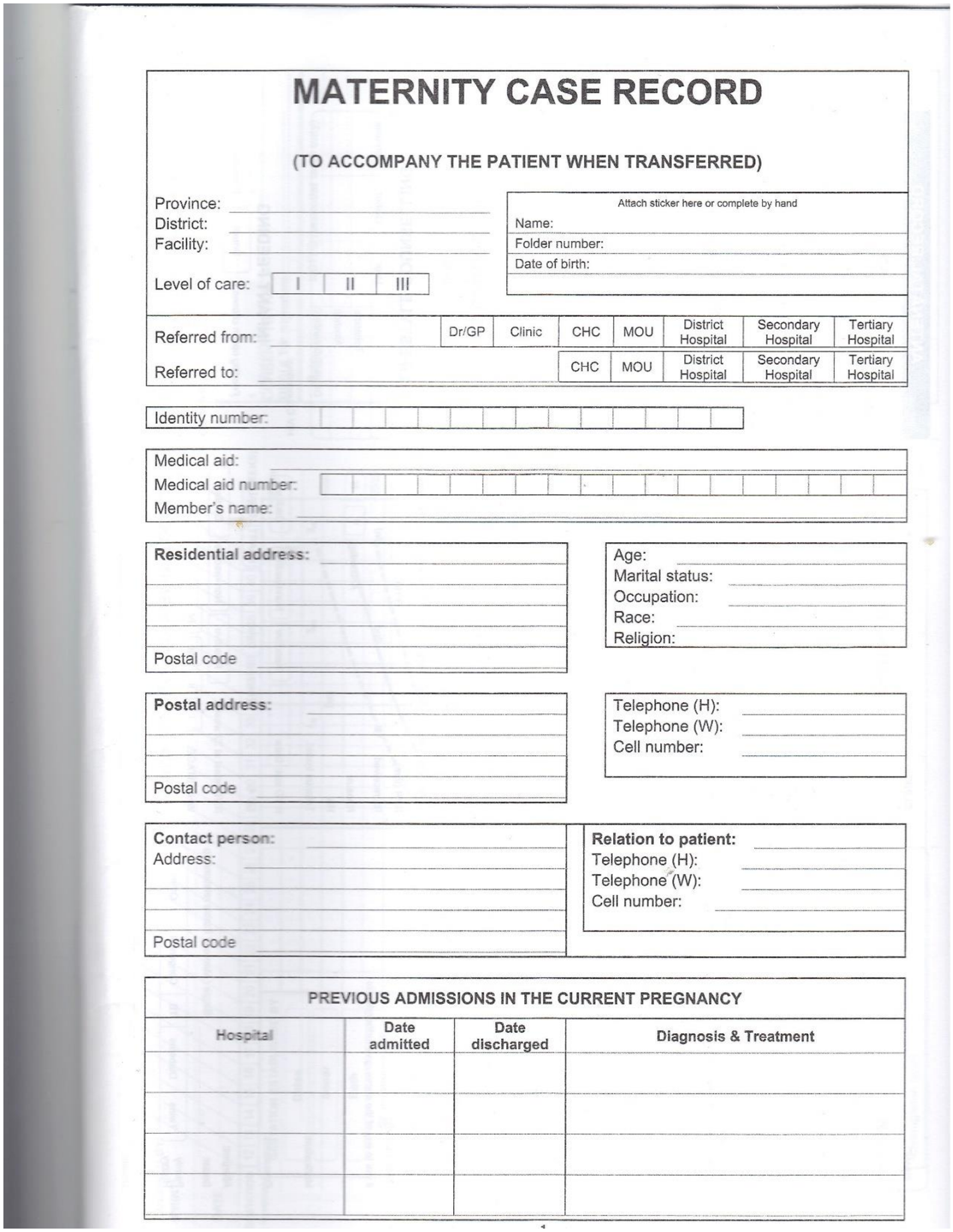
Test today, result later

Test delayed

Test declined

Post-test counselling

Appendix 5: Maternal Case Record file



MATERNITY CASE RECORD

(TO ACCOMPANY THE PATIENT WHEN TRANSFERRED)

Province:
District:
Facility:

Level of care: I II III

Attach sticker here or complete by hand

Name:
Folder number:
Date of birth:

Referred from:	Dr/GP	Clinic	CHC	MOU	District Hospital	Secondary Hospital	Tertiary Hospital
Referred to:			CHC	MOU	District Hospital	Secondary Hospital	Tertiary Hospital

Identity number:

Medical aid:
Medical aid number:
Member's name:

Residential address:
Postal code

Age:
Marital status:
Occupation:
Race:
Religion:

Postal address:
Postal code

Telephone (H):
Telephone (W):
Cell number:

Contact person:
Address:
Postal code

Relation to patient:
Telephone (H):
Telephone (W):
Cell number:

PREVIOUS ADMISSIONS IN THE CURRENT PREGNANCY

Hospital	Date admitted	Date discharged	Diagnosis & Treatment

NAME:

FOLDER NO:

DATE OF BIRTH:

Address:

Postal code: Tel:

Age: (yrs) G P Misc

OBSTETRIC & NEONATAL HISTORY A = Alive ID = Infant Death NND = Neonatal Death IUD = Intra-uterine Death

Year	Gestation	Delivery	Weight	Sex	Complications

Descriptions of complications:

MEDICAL & GENERAL HISTORY

Hypertension	Epilepsy	Diabetes	Cardiac	TB	Healthy

Other (specify)

If yes to any of the above, give further details:

Medication:

Operations:

Allergies:

Social: Single / Married / Stable relationship

Family History: Twins | Diabetes | TB | Congenital | Other

Details:

CLINIC

EXAMINATION

Date d d m m y y BP /

Height cm Weight kg

Thyroid: Breasts:

Urine:

Heart:

Lungs:

Abdomen:

Other: MUAC: BMI:

SF measurement cm Correlation with dates? Y N

VAGINAL EXAMINATION

Done | Not done

Vulva & Vagina:

Cervix:

Uterus:

Pap Smear done? Y N Date:

Result:

INVESTIGATIONS

Rapid syphilis test: Pos Neg Repeat syphilis test: Pos Neg

RPR (titre): TPHA:

Rx received: 1st 2nd 3rd

Rhesus: Antibodies: Y N

Hb: g/dl

Tetanus toxoid: 1st 2nd 3rd

RVD test: Date: Reactive Non-reactive Declined

CD 4: Therapy: Date: HAART DUAL

RVD retest at 32 weeks: Reactive Non-reactive Declined

WHO STAGE: I II III IV

OTHER INVESTIGATIONS/PROTOCOLS

ANTENATAL RECORD

PLAN

Antenatal care:	Labour or 36+ weeks
Transport:	

DATES

LNMP d d m m y y Certain? Y N

ULTRASOUND

Date:

BPD

FL

Abd. Circ.

Placenta

Other

EDD

d d m m y y According to: Dates | U/S | SF height

FUTURE CONTRACEPTION

Injectable | Oral | IUCD | T/L | Dual Protection

LIFESTYLE COUNSELLING

	User	Quitter	Non-user
Tobacco:			
Alcohol:			
Drugs/Substances:			

HIV Counselling:

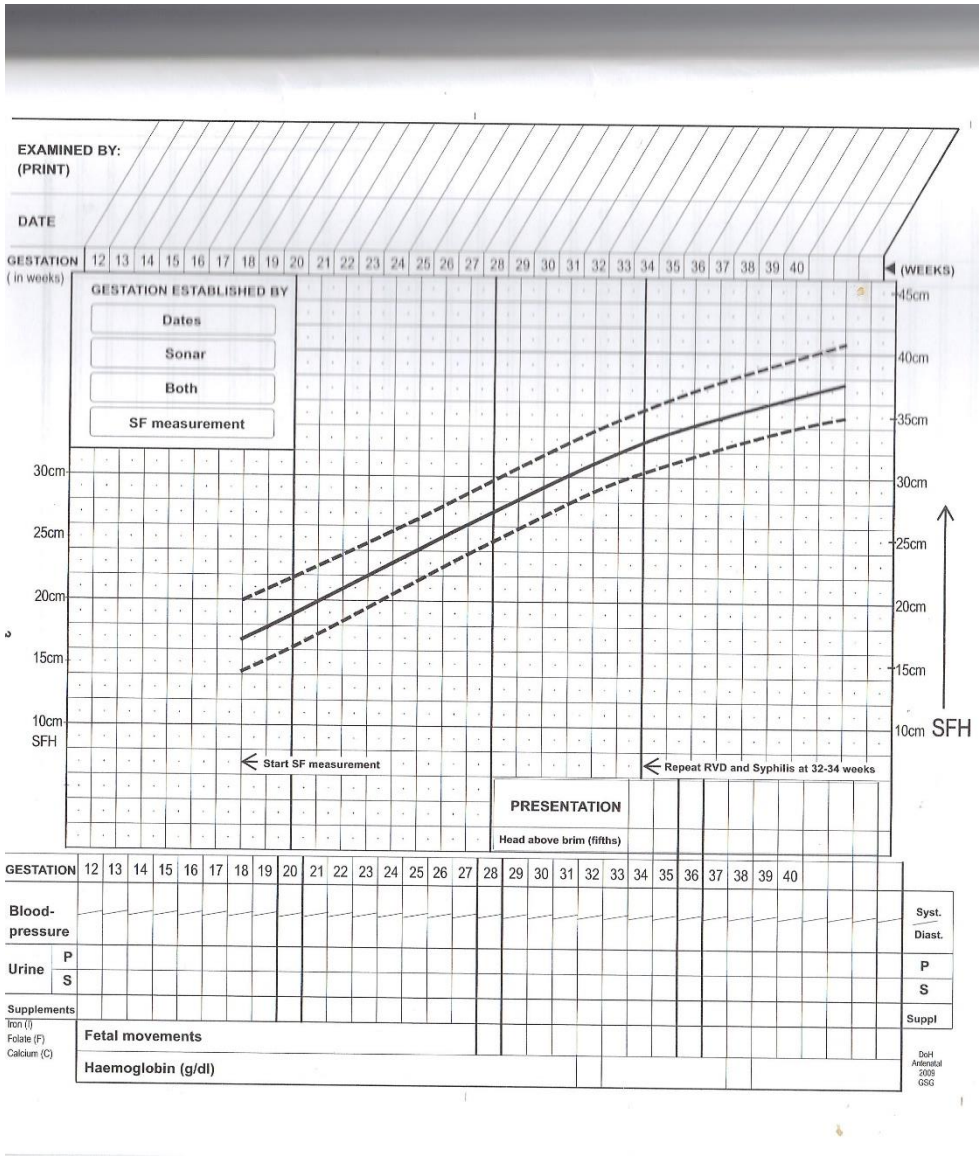
INFANT FEEDING

Feeding option chosen: Breast | Formula

Comments:

Booking visit and Assessment of Risk done by:

Name & Title



Date	PROBLEM LIST
1	
2	
3	
4	
5	

CONSENT TO RVD
RESULTS: signature.....

Date	NOTES (essential facts only)

Appendix 6: Case/control record

Study number	Cases			Control		
	Hospital number	Age of mother	Sex of baby	Hospital number	Age of mother	Sex of baby

References

[1] Barium MZ, Deseret Z, Nauru M. Incidence and correlates of low birth weight in Northwest Ethiopia. Pan African Medical Journal 2012; 12:4.

[2] Career B, Linda M, Kenneth M. Risk factors for low birth weight in a public hospital in Peshawar. BMC public health 2008; 8:197.

[3] Catia RB, Strufaldi MW, Carvalho LR. Risk factors for low birth weight in Botucatu city, SP state Brazil: a study conducted in the public health system from 2004 to 2008. BMC Research Notes 2012; 5:60.

[4] Rizvi SA, Hatcher J, Jehan I, Qureshi R. Maternal risk factors associated with low birth weight Karachi: a case- control study. Eastern Mediterranean Health Journal 2007; 13:6.

[5] Batist SE. A case-control study of factors for low birth weight in the Western Cape Winelands/west coast region [dissertation]. University of Western Cape. 2003.

[6] Faten MR, Ismaeil H, Al Musa HM. Prevalence and determinants of low birth weight in Abha city Ksa. Life Science Journal 2012; 9 (4).

[7] Chiavaroli V, Castoran V, Guidone P, Derraik JGB, Liberati M, Chiarelli F, et al. Incidence of infants born small-and large –for-gestational-age in an Italian cohort over a 20-year period and associated risk factors. Italian Journal of Paediatrics. 2016; 24 (42).

[8] Bong JL, Lim SH. Risk of low birth weight associated with family poverty in Korea. Children and Youth Services Review; 2010 (32): 1670-1674.

[9] District Health Information System. Low birth weight rate. Health system trust. Available from: URL: http://indicators.hst.org.za/healthstats/153/data . Accessed 3/05/13.

[10] Hummer M, Lehner T, Pruckner G. Low birth weight and health expenditure from birth to late adolescence. Eur J Health; 2013 April.

[11] Siza J E. Risk factors associated with low birth weight of neonate among pregnant women attending a referral hospital in northern Tanzania. Tanzania Journal of Health Research; 2008 (10) 1.

[12] Velaphi SC, Mokhachane M. Survival of very low birth weight infants according to weight and gestational age in a public hospital. S Afr Med J 2005; 95:504-509.

[13] Hummer M, Lehner T, Pruckner G. Low birth weight and health expenditure from birth to late adolescence. Eur J Health. 2013 April.

[14]Izunwa RD. Factors that Predispose to low birth weight in Makana District, Eastern Cape, South Africa [thesis]. University of Medunsa; 2008.

[15] Bayingana C, Muvunyi CM, Africa CW. Risk factors of preterm delivery of low birth weight (plbw) in an African Population. Journal of Clinical Medicine and Research. 2010 July; 2(7): 114-118.

[16] Braganca de Moraes A, Zanini RR, Elsa RG. Risk factors for low birth weight in Rio Grande do Sul State, Brazil: classical and multilevel analysis. Cad Saude Publica, Rio de Janeiro 2012 Dec. 28; 12:2293-2305.

[17] Teagle Andres. Refugees: Out of the frying pan and into the fire of South Africa's healthcare system. Daily Maverick 2014 October 16.

[18] Lindsay AT, David CG, Chiang-Hua C, Therese AS. Regional variation in rates of low birth weight. J Paediatrics 2005; 116:5.

[19] Shabet F, Richter L, Ramchandani PG, Stein A, Quigley MA, Norris SA. Low birth weight and subsequent emotional and behavioral outcome in twelve year-old children in Soweto, South Africa: Findings from birth to twenty. International Journal of epidemiology 2009; 38:944-954.

[20] Sutan R, Mothar M, Mahat AN, Tamil AM. Determinant of Low Birth Weight Infants: A Matched Case Control Study. Open Journal of Preventive Medicine [serial online] 2014 [cited 2016 October 10]; 4: 91-99. Available from: http://dxdoi.org/10.4236/oipm.2014.43013.

[21] Javier V, Trinidad S, Romana A, et al. Risk factor for low birth weight: A review. European Journal of Obstetrics & Gynecology and reproductive biology 2004; 116:3-15.

[22] UNICEF, WHO, Low Birth weight Country, Regional and Global Estimates. Available from: URL: http://www.childinfo.org/files/low_birthweight_from_EY.pdf *Accessed 5/06/13.*

[23] Hughes MM, Black RE, Katx J. 2500-g Low Birth Weight Cut-off: History and Implications for Future research and Policy. Matern Child Health J [serial online] 2016 July [cited October]; Available from Maternal and Child Health.

[24] Zambonato AMK, Pinheiro RT, Horta BL, Tomasi E. Risk factors for small-for-gestational age births among infants in Brazil. Rev Saude Publica 2004; 38(1).

[25] Lee AC, Katz J, Blencowe H, Cousens S, Kozuki N, Vogel HP, et al. National and regional estimates of term and preterm babies born small for gestational age in 138 low-income and middle- income countries in 2010. Lancent global Health 2013 July; 1.

[26] Kramer MS. Determinants of low birth weight: Methodological assessment and meta-analysis. Bulletin of the World Health Organization1987; 65 (5):663-737.

[27] Javier V, Trinidad S, Romana A, et al. Risk factor for low birth weight: A review. European Journal of Obstetrics & gynecology and reproductive biology 2004; 116:3-15.

[28] Gail B S, Schwartz JS. Risk Factors for low birth weight to Adolescent Mothers. Journal of adolescent health care 1989; 10:267-274.

[29] Institute of Health Economics (Alberta, Canada). Determinants and Prevention of Low Birth Weight: A Synopsis of the Evidence. Institute of Health Economics; 2008.

[30] Bolajoko O. O, Gabriel E. O. Predictors of Pre-term births and low birth weight in an inner city hospital in sub-Sahara Africa. Matern Child Health J 2010; 14:978-986.

[31] Gobopamang L, Rolang GM. Factors Influencing low birth weight and prematurity in Botswana. J biosoc. Sci 2001; 33:391-403.

[32] Oliver LTV. Study on factors associated with low birth weight at Uitenhage Hospital [dissertation]: University of Western Cape; 2000.

[33] Yihua B, Zhan Z, Qiao Liu, Di W, Shoulin W. Maternal risk factors for low birth weight in a developed region in C: a hospital-based study of 55,633 pregnancies. Journal of biomedical Research 2013; 27(1):14-22.

[34] John WP, Paul JG, Are Clinical criteria just proxies for socioeconomic status? A study of low birth weight in Jamaica. Journal of Epidemiology and Community Health 1997; 51:90-95.

[35] Tierney-Gumaer R, Reifsnider E. Risk factors for low birth weight infants of Hispanic, African American, and white women in Bexar County, Texas. Public Health Nursing 2008; 25:5: 3900-4000.

[36] Racape J, Schoenborn C, Sow M, Alexander S, De Spiegelare M. Are all immigrant mothers really at risk of low birth weight and perinatal mortality? The crucial role of Socio-economic Status. BMC pregnancy and Childbirth. 2016; 75(16).

[37] Ndirangu J, Newell Ml, Bland RM, Thorne C. Maternal HIV infection associated with small-for-gestational age infants but not preterm births: evidence from rural South Africa. Human reproduction. 2012; 27(6): 1846-1856.

[38] Moodley S, Buchmann E. Outcome of Very Low Birth Weight Babies Born to HIV Positive Mothers. [dissertation]. University of Witwatersrand; 2013.

[39] Dharmaligam A, Navaneetham, Krishnakumar CS. Nutritional Status of mother and low birth weight in India. Matern Child Health J 2010; 14:290-298.

[40] McCowan L, Horgan RP. Risk factors for gestational age infants. Best Practice & Research Clinical Obstetrics and Gynaecology. 2009; 23: 779-793.

[41] Rosalie T, Reifsnider E. risk factors for low birth weight infants of Hispanic, African American, and white women in Bexar County, Texas. Public Health Nursing 2008; 25:5: 3900-4000.

[42] Muhihi A, Sudfeld CR, Smith ER, Noor RA, Mshamu S, Briegleb C, et al. Risk factors for small-for –gestational-age and preterm births among 19,269 Tanzanian newborns. BMC pregnancy and Childbirth 2016; (16) 110.

[43] Taylor L, Yi Cathy Y, Lim K, Simpson JM, Roberts C, Morris J. Potential prevention of small for gestational age in Australia: a population-based linkage study. BMC pregnancy and Childbirth. 2013; (13) 210.

[44] Gauteng Department of Health. South Rand hospital Patient Profile. Available from : URL: http://www.health.gpg.gov.za. Accessed 10/03/17.

[45] Nagargoje M, Chaudhary S, Deshmukh J S, Gupta S K. A Case control study for risk factors of low birth weight in Nagpur city of Maharashtra. Indian journal of community health 2011; 23:1.

[46] National dept. of Health. National antenatal sentinel HIV and syphilis prevalence survey in South Africa. Available from: URL: http://www.doh.gov.za/docs/.../Antenatal_Sentinel_survey_Report2012_final.p... *Accessed 3/6/13.*

[47] Gabriel C, Flash S, Deoich Y, Varda S. Seasonality in Birth Weight: Review of global patterns and potential Causes. Human Biology. 2009; 81 (4) 463-477.

[48] Coutinho PR, Cecatti JG, Surita FG, PaAulo de Souza J, Siani de Marais. Factors associated with Low Birth Weight in a Historical Series of Deliveries in Campinas, Brazil. Rev Assoc Med Bras 2009; 55(6): 692-699.

[49] Sharma SR, Giri S, Timalsina U, Bhandari SS, Basyal B, Wagle K, et al. Low Birth Weight at term and its Determinants in a Tertiary Hospital of Nepal: A Case-control Study. Journal Pone [serial online].2015 [cited 2016 October 10]. Available from PLOS one.

[50] Bhaskar RK, Deo KK, Neupane U, Bhaskar C, Yadav BK, Pokharel HP, et al. A Case Control Study on Risk Factors Associated with Low Birth Weight babies in Eastern Nepal. International Journal of Paediatrics. 2015.

[51] Yadav H. Maternal Factors in Predicting Low Birth Weight Babies. Med J Malaysia. 2013 Feb; 68 (1).

[52] Demelash H, Motbainor A, Nigatu D, Gashaw K, Melese A. Risk factors for low birth weight in Bale zone hospitals, Sout-East Ethiopia: a case-control study. BMC pregnancy and Childbirth. 2015; (264): 15.

[53] Kumar SG, Kumar HNH, Jayaram S, Kotian MS. Determinants of Low Birth weight: A Case Control Study in a District Hospital in Karnataka. Indian Journal of Paediatrics. 2010; 77.

[54] Mumbrare S, Maindarkar G, Darade R, Yenge S, Tolani KM, Patole K. Maternal Risk Factors Associated with Term Low birth Weight Neonates: A matched-pair Case Control Study. Indian Paediatrics. 2012; 49.

[55] Delgano-Rodriguez M, Perez-Iglesias R, Gomez-Olmedo M, Bueno-Cavanillas, Galvez-Vargas R. Risk Factors for Low Birth Weight: Result From a Case-Control Study in Southern Spain. American Journal of Physical Anthropology. 1998; 105: 419-424.

[56] Tunny S, Yadav B, Jeyaseelan L, Vijayaselvi R, Jose R. Small for gestational age births among South Indian women: temporal trend and risk factors from 1996 to 2010. BMC Pregnancy and Childbirth. 2015; 15(7).

[57] Ota E, Ganchimeg T, Morisaki N, Vogel JP, Pileggi C, Ortiz-Panoza E, et al. Risk factors and Adverse Perinatal Outcomes among Term and preterm Infants Born Small-for-Gestational age: Secondary analyses of the WHO Multi-country Survey on Maternal and Newborn Health. Plos one. 2014; 9 (8):

[58] Xiao P, Zhou Y, Chen Y, Yang M, Snog X, Shi Y, et al. Association between maternal HIV infection and low birth weight and prematurity: a meta-analysis of cohort studies. BMC Pregnancy and Childbirth. 2015; 246 (15).

[59] Diaz LM, Dinsmoor J M, Lin PY. Preventable risk factors for the delivery of very low birth weight infants in Richmond, Virginia. Prim care update. Ob/Gyns. 2001; 8 (1.)

60 American College of Obstetrician and Gynaecology. Committee opinion. Available from : URL:
http://www.acog.org. Accessed 10/03/17.