A RETROSPECTIVE SOUTH AFRICAN STUDY OF PATIENT CHARACTERISTICS AND PREGNANCY OUTCOMES IN A COHORT OF WOMEN ACROSS VARIOUS BODY MASS INDEX CATEGORIES

by

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Supervisor Declaration

Supervisor: Dr Samantha Budhram

As the candidate's supervisor I have approved this thesis for submission.

Signed: _____ Name: Dr Samantha.Budhram

Date: 25/11/2021

Student Declaration

I, Dr Payal Sewmungal , declare that:

(i) The research reported in this dissertation, except where otherwise indicated, is my original work.

(ii) This dissertation has not been submitted for any degree or examination at any other university.

(iii) This dissertation does not contain other persons' data, pictures, graphs or other information, unless specifically acknowledged as being sourced from other persons.

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Executive summary

Introduction: South Africa, a low- and middle-income country, has not been spared by the obesity epidemic and is especially challenged by an exponentially growing population of overweight and obese women. Pregnancy is a risk factor for obesity and vice versa. Body mass index (BMI) on either end of the spectrum may complicate pregnancies and impact on maternal and fetal outcomes. Little is known about these outcomes in a local context.

Aim of study: To describe and compare the demographics, clinical characteristics, clinical course and outcomes of pregnant women across different BMI categories.

Methods: This retrospective study included data from consecutive medical records of women with singleton pregnancies, who had an obstetric ultrasound examination before 24weeks of gestation and who delivered during the period 1 January 2017 to 31 July 2017 at General Justice Gizenga Mpanza Regional Hospital. The cohort was divided into groups according to the maternal BMI. An analysis of variants (ANOVA) (F-Test) was used to determine if there were differences in patient characteristics and pregnancy outcomes among women in different BMI categories. A *p*-value of < 0.05 was considered significant.

Results: The cohort consisted of 993 women of which the majority, 918(92.7%), were ethnically Black African with a median age of 25years and a median BMI of 26.2kg/m^2. According to BMI categories, 31(3.1%) women were under-weight and just under one-third(28.6%) were obese. There was an increasing prevalence of comorbidities, caesarean deliveries and heavier offspring birthweights with increasing maternal BMI ($p < 0.01$). Co-existence of obesity and HIV-infection was seen in 134(47%) women while being overweight and HIV-infection co-existed in 121(43%) women in the cohort ($p = 0.043$).

Conclusion and recommendations: Overweight and obese pregnant women showed a higher prevalence of HIV-infection, chronic hypertension, caesarean delivery and larger offspring compared to their normal and under-weight counterparts. This highlights the growing burden of obesity as a non-communicable disease and its future health implications for reproductive-aged women. Our recommendations are that public health programs and initiatives be directed towards; identifying at-risk reproductive-aged women, enrolment in pre-pregnancy clinics, support with sustainable weight-loss, exercise and dietary programs, ongoing community education on healthy food choices and active lifestyles, encouraging planned pregnancies, long-term non-hormonal contraception promotion during weight optimisation and destigmatisation of chronic diseases like human immuno-deficiency virus infection.

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Chapter 1

Introduction

Obesity is a rapidly emerging health problem with the prevalence having nearly tripled globally between 1975 and 2016[1]. Associated with, and paralleling the obesity epidemic, is an upsurge in the incidence of non-communicable diseases[1]. South Africa (SA), a low- and middle-income country (LMIC), has not been spared by the obesity epidemic and is especially challenged by an exponentially growing population of overweight and obese women. A South African demographic and health survey reported that 68% of women aged 15years and older were overweight or obese[2].

Several risk factors have been identified for obesity which include; urbanisation, sedentary lifestyle, cheap and readily available carbohydrate-rich foods, genetic predisposition and poor socioeconomic status[3,4]. In Durban, SA, being overweight or obese has been shown to be more prevalent among urban, ethnic black women living in areas of high human immune-deficiency virus (HIV) infection prevalence[5]. Cultural and traditional perceptions that being overweight or obese is a desirable reflection of good health and higher socioeconomic status[3,4] and the contrary, being lean or under-weight, is associated with HIV-infection or acquired immuno-deficiency syndrome (AIDS), are drivers of obesity in communities[6].

Pregnancy is a risk factor for obesity and vice versa[7]. Body Mass Index (BMI), a measure indicating nutritional status in adults is defined as a person's weight in kilograms divided by the square of the person's height in metres (kg/m^2). BMI on either end of the spectrum may complicate pregnancies and impact on maternal and fetal outcomes. Excessive gestational weight gain can contribute to postpartum weight retention contributing to the continuum of high pre-pregnancy BMI[7].

Maternal risks of obesity include; a higher incidence of comorbid disease e.g. gestational diabetes, preeclampsia, gestational hypertension, depression, instrumental and operative vaginal delivery and caesarean delivery[7-9]. Adverse fetal outcomes include; congenital abnormalities, large for gestational age fetuses and

macrosomia[9,10]. Under-weight pregnant mothers have been shown to have an increased risk of preterm delivery and low birthweight neonates[11]. Limited data exists from SA of pregnancies in women of different BMI categories and their respective outcomes.

Chapter 2: Literature review

2.1. Global incidence and prevalence

Weight challenges of pregnant and reproductive-aged women is an escalating, poorly managed health burden of public interest. Globally, we have witnessed a change in human body habitus over the last few decades with a transition from being underweight to overweight[12]. The proportion of over-weight women increased from approximately 30% to almost 40% between the years 1980 and 2013[13]. The combination of a pregnant state and being over-weight or obese has been shown to be associated with a higher risk of severe morbidity and mortality[13]. The incidence varies worldwide based on socioeconomic status, level of urbanisation and ethnicity.

2.2. South African prevalence

The South African Demographic Health Survey of 2016 reported 30% of women to have a BMI in the normal range, 3% were under-weight, 27% over-weight and 41% were obese, of which 20% were severely obese[2]. The mean BMI increased from 27.3kg/m^2 to 29.2kg/m^2 from 1998 to 2016 while in this same period the prevalence of underweight women decreased from 6% to 3% and overweight and obese women increased from 56% to 68%[2]. Current projections suggest a significant rise in BMI in sub-Saharan Africa over next few decades[14] with driving factors identified as being; genetic predisposition, African ethnicity, fatty diets, sedentary lifestyles and low socioeconomic status[13].

2.3. BMI category and associated outcomes in pregnancy

Maternal underweight has been associated with a small increase in preterm delivery, lower offspring birthweight and higher incidences of preeclampsia, gestational diabetes mellitus and obstetric interventions[11]. On the contrary increased incidences of hypertension, preeclampsia, gestational diabetes, and adverse fetal outcomes such as congenital abnormalities, fetal and neonatal death have been reported in obese pregnant women[9].

Several studies have focused on specific categories of BMI e.g. under-weight, obese or super-obese. The pregnancy outcomes explored have been limited to either maternal or fetal outcomes. Maternal outcomes included prevalence of; gestational diabetes and hypertension, preeclampsia, depression, instrumental versus operative mode of delivery, surgical-site infection and fetal outcomes encompassing birthweight with special emphasis on macrosomia and large for gestational age fetuses, congenital abnormalities and perinatal death[8,9,15]. There are no studies published in SA that have addressed all maternal BMI categories and their association with maternal and fetal outcomes, if any.

2.4. Pregnancy outcomes in similar socio-economic settings as SA.

Two studies in similar socioeconomic settings, conducted in Ghana[10] and Goa[16] analysed data on maternal BMI and pregnancy outcomes. Both studies demonstrated similar findings of overweight and obesity being associated with higher caesarean delivery rates, gestational diabetes mellitus and macrosomia[10,16]. Despite the conclusions being similar for the obese group, the study in Ghana was a prospective study comprising of 824 women with a mean age of 28years, 31,3% overweight and 16,9% obese women in comparison to the study in Goa which was retrospective with 100 primigravidae aged between 24 and 30years, 22% overweight and 10% were obese[10,16]. The similarities in both these studies were cohorts of similar ages and socioeconomic groups, however they differed in terms of a known pre-pregnancy BMI versus a BMI calculated at first antenatal clinic visit. Only primigravidae were included in both studies and sample sizes were skewed[10,16].

2.5. Pregnancy outcomes reported in South African literature

Two local studies have reported maternal and fetal outcomes focusing predominantly on obese women. A cross-sectional study conducted at Charlotte Maxeke Johannesburg Academic Hospital in Gauteng, SA was aimed at determining the prevalence of obesity and its effect on maternal and fetal outcomes. The proportion of women classified as obese or morbidly obese was 44%, 94% were of Black African ethnicity and they reported no significant difference in offspring birthweights among maternal BMI groups[17]. The study was limited by the non-inclusion of an underweight maternal BMI category to make a comparison to, the gestational ages

of the pregnant women were not accurately determined due to late-booking with a mean gestational age at booking of 28weeks. The authors conceded that late-booking may have prevented early management of antenatal complications and also had implications on reported birthweights[17]. Evidence to the contrary, reported in another case-control study conducted in the obstetric special care clinic at Tygerberg Hospital in the Western Cape, showed that babies born to morbidly obese mothers were heavier than babies born to women with a normal BMI[18]. Another prospective cohort study also conducted in the same facility noted that intrauterine growth restriction was greater in the super-obese (BMI $\geq$ 50kg/m^2) women with an increased risk of extremely low-birthweight neonates in obese women[15].

Pregnancy outcomes focusing on the mode of delivery has been reported in a large retrospective study of 752 deliveries, conducted in Johannesburg, SA. It showed a higher rate of assisted and caesarean deliveries in morbidly obese women compared those in other BMI categories and similar rates of caesarean delivery in the normal and obese BMI categories of 48.3% vs 48.1% respectively, however, this was statistically not significant (p = 0.15)[17].

2.6. Patient Demographics and clinical characteristics

Reports of patient demographics and clinical characteristics (age, race, gravidity and parity, pre-existing comorbidities and social habits) were not included in any of the studies reviewed.

2.7. BMI and HIV-infection

The 2017 National Antenatal Sentinel HIV survey reported a prevalence of HIV-infection of 41.1% among antenatal clinic attendees in Kwazulu-Natal, SA[12]. The prevalence of HIV-infection has been shown to be higher in women of higher BMI categories with possible reasons cited as; attempts by women to defy the stigma of leanness being associated with HIV/AIDS and cultural beliefs that rounder physique is positively connotated with ‘good’ health[3,4,6]. There are no South African studies correlating maternal BMI categories and HIV-infection.

2.8. Patient comorbid medical conditions

A clear relationship has been documented between increasing BMI and; the risk of gestational hypertension, preeclampsia and gestational diabetes[8,20]. There is a linear relationship noted with increasing BMI and hypertensive disorders of pregnancy[18]. Obesity and preeclampsia are similar in their association to oxidative stress with increased circulating inflammatory markers: acute phase reactants, C-reactive protein, and inflammatory cytokines (tumour necrosis alpha, interleukin- 6 and 8) being common to both conditions[20]. This may provide the basis for the relatively common occurrence of both conditions in the same patient.

2.9. Modes and timing of delivery across BMI categories

Increased instrumental vaginal delivery and caesarean deliveries are associated with higher BMI categories[8,20]. This has been postulated to be as a result of increased deposition of cholesterol in the myometrial tissue of obese women impacting adversely on myometrial contractility. In addition, excessive adipose tissue found along the birth canal of obese women may narrow the passage and pose a greater challenge for delivery of larger offspring[8].

The pooled results of a systematic review showed an increase in spontaneous preterm birth in overweight and obese women as well as an increase in rates of post-datism and need for induction of labour and augmentation of labour in obese women[8].

2.10. BMI and future potential maternal risks :

The burden of overweight and obesity and increasing rates of caesarean delivery remains unabated and with it comes further risks of repeat operative delivery with its attendant complications. This poses new challenges for subsequent pregnancies with increased BMI and a previous caesarean section. These include obstetric surgical-related risks of difficult repeat caesarean section due to loss of anatomical landmarks and arduous abdominal entry and greater risk of postpartum haemorrhage. This is further compounded by anaesthetic related risks of fluid retention and stasis, excessive lung secretions, poor ambulation peri- and post-operatively leading to increasing thromboembolic risk[21,22]. Other post-operative

complications include prolonged hospital-stay due to increased risk of local wound sepsis due to warmth and moisture beneath the pannus and hypostatic pneumonia[22].

2.11. BMI and future potential offspring risks

Maternal obesity is associated with epigenetic remodelling with alterations in DNA methylation in sites linked with offspring adiposity hence higher maternal BMI has an effect on offspring metabolic outcomes and increases the risk for excessive adipose accumulation, larger for gestational age and obesity during childhood and adolescence[23-25] . This poses a further public health concern as one would expect that paralleling the growing obese child and adolescent population is a greater burden of non-communicable diseases.

2.12. Off-spring birthweight across BMI categories

In overweight and obese women there is decreased risk of low birth weight and increased risk for large for gestational age and macrosomic off-spring compared to women of normal weight[8]. Macrosomia ($\geq$ 4000g) was more prevalent in the overweight and obese groups compared to the normal BMI groups[20]. Low birth-weight offspring were associated with maternal underweight[26] .

2.13. Relevance of this study

The obesity epidemic has not spared South Africa and reproductive-aged women appear to be more affected than their male counterparts. This situation has translated into having greater proportions of women with higher BMI falling pregnant. The maternal and fetal risks have been well described in extremes of maternal BMI yet there is paucity of data in a South African population

2.14. Purpose of this study

Given the scarcity of literature on pregnancy courses and outcomes in different maternal BMI categories in SA, the purpose of this study is to bridge the gap in knowledge to enable us to better manage these conditions. This research is

essential to inform clinical guidance on the management of pregnant women in a local setting as well as to formulate public health policy.

2.14.1 Aims of this study

To describe demographics, clinical characteristics and the course and outcomes of pregnancies of women across BMI categories who delivered at the General Justice Gizenga Mpanza Regional Hospital in Kwa-Dukuza, SA.

2.14.2. Objectives of this study

i. To compare the demographics and clinical characteristics of the cohort across BMI categories
   - Age
   - Race
   - Parity
   - HIV-infection

ii. To compare the comorbid medical conditions of the cohort across BMI categories
   - Hypertension
   - Diabetes mellitus
   - HIV-infection

iii. To compare the rates of modes of delivery of the women across BMI categories
   - Elective caesarean section
   - Emergency caesarean section
   - Induction of labour

iv. To compare offspring birthweight cohort across the BMI categories

v. To determine number of macrosomic babies born to women across the BMI categories.

Chapter 3

Methodology

3.1. Site of study: The study site was General Justice Gizenga Mpanza Regional Hospital (previously Stanger Hospital). General Justice Gizenga Mpanza Regional Hospital is a 500-bedded regional and district hospital located in Kwa-Dukuza within the Ilembe Health District in Kwazulu Natal (KZN), SA. The hospital serves an estimated population of 600 000 from the Ilembe District. This site was chosen to conduct the study acknowledging; the array of different socioeconomic backgrounds, the presence of an accredited in-facility obstetric sonographer and the relatively high delivery rate (650 deliveries/month).

3.2. Study design

Descriptive retrospective chart review

3.3. Study population

All women with singleton live pregnancies having undergone an obstetric ultrasound examination before 24 weeks of gestation and who delivered during the period 1 January 2017 to 31 July 2017 at the Stanger Regional Hospital.

3.4. Study period

1 January 2017 to 31 July 2017

3.5. Sample size, sample selection and subjects

The sample size planned was 1000. The statistically estimated sample size taking into consideration time, achievability and practicality was a minimum of 908.

The statistical parameters:

1. Determining minimum sample size with statistical power of 80%
2. A small effect size of 0,11

3. Type I Error (α) = (0,05) This is the probability of a false positive
4. Type II Error (β) = (0,2) This is the probability of a false negative

On the basis of the above mentioned statistical parameters, a minimum size of 908 was determined.

Records of all women who delivered consecutively during the period 1 January 2017 to 31 July 2017 and satisfied the inclusion and exclusion criteria were selected for the study.

Inclusion Criteria

1. Singleton pregnancy
2. A live foetus at booking visit
3. An ultrasound dating of the pregnancy at gestational age at ≤ 24 weeks performed by an accredited sonographer.

Exclusion Criteria

1. Suspected or confirmed foetal anomaly
2. Missing data for calculation of BMI

3.6. Data collection

Once ethical approval was obtained from the University of KZN's Biomedical Research Ethics Committee (Appendix 2) and permission granted by the Chief Executive Officer General Justice Gizenga Mpanza Regional Hospital (Appendix 3), data collection was commenced.

The hospital maternity registry was searched for records of all women who delivered consecutively for the study period and met inclusion and exclusion criteria. Each patient was allocated a unique study number for the purposes of data collection and in order to maintain patient confidentiality. Data was collected on a structured predesigned data collection sheet (Appendix 1). All data collected was verified prior to being captured on a Microsoft Excel spread-sheet.

3.7. Data analysis

Data was analysed with the assistance of a statistician. Continuous variables such as patient ages and weight were summarised as mean +/- standard deviation or median inter-quartile range (IQR) as appropriate and compared using Student T-test or Wilcoxon–Mann-Whitney Test as appropriate.

Categorical variables, such as comorbidities and social habits (drug, alcohol or tobacco use) was summarised as percentages and proportions and compared using Chi-squared test or Fishers exact test as appropriate.

A one way ANOVA was used to compare patient outcomes among BMI categories. All analyses were conducted using IBM SPSS version 25 and level of significance kept at $p < 0.05$.

3.8. Definitions used for the purpose of this study

3.8.1. Body mass index is weight in kilograms divided by the square of height in meters (kg/m^2).

3.8.2. BMI categories:

- Underweight < $18.5kg/m^2$
- Normal 18.5 – $24.9kg/m^2$
- Overweight 25.0 - $29.9kg/m^2$
- Obese ≥ $30kg/m^2$
    - Obesity Class I 30 - $34.9kg/m^2$
    - Obesity Class II 35 - $39.9kg/m^2$
    - Obesity Class III ≥ $40kg/m^2$

3.8.3. Term pregnancy – Gestational age of 37 weeks 0 days to 41 weeks 6 days

3.8.4. Preterm - Gestational age < 37 weeks 0 days

3.8.5. Post-term – Gestational age ≥ 42 weeks 0 days

3.8.6. Macrosomia – birthweight ≥ 4000g

3.8.7. Chronic hypertension – hypertension predating pregnancy or diagnosed before 20 weeks of gestational age

3.8.8. Comorbidity - any pre-existing medical condition at booking of antenatal care

3.8.9. Maternal mortality – death of a female from any cause related to or aggravated by pregnancy or its management, excluding accidental or incidental causes, during pregnancy or childbirth or within 42 days of termination of pregnancy, irrespective of the duration and site of the pregnancy

3.8.10. Booking visit - first consultation with healthcare provider for antenatal care

3.8.11. State-subsidized facilities - government owned, administrated and controlled facilities. Facilities funded by the government and operates solely off money collected from taxpayers to fund healthcare initiatives

Chapter 4

Results

The study cohort comprised of 993 women. The ethnicity of the majority of women was African (n = 918, 92.7%) while the rest of the cohort was made up of Indians (n = 50, 5.0%), Coloureds (n = 18, 1.8%) and Caucasians (n = 7, 0.7%). The median age of the cohort was 25 years (range 14 – 44), parity of 1 (range 1 - 8) and BMI of 26.2kg/m^2 (range 14.7 – 57.7) (Table 1). Pre-existing medical conditions included chronic hypertension, diabetes mellitus, HIV-infection, anaemia, epilepsy, cardiac disease and chronic kidney disease. Seventy (0.7%) of the cohort had a diagnosis of chronic hypertension, 6,7% were overweight and 10.9% were obese, $p = 0.011$ (Figure 1). HIV-infected women accounted for 42.5% of the entire cohort, all of whom were on antiretroviral therapy. Co-existence of obesity and HIV infection was seen in 134 (47%) women while being overweight and HIV infection co-existed in 121 (43%) women in the cohort ($p = 0.043$).

The overall rate of caesarean delivery in the cohort was 34.7%. Emergency and elective caesarean sections accounted for 247 (24.9%) and 98 (9.9%) of all deliveries, respectively. Within each BMI category, emergency caesarean sections were performed in 4 (12.9%) underweight, 84 (21.3%) normal weight, 73 (25.7%) overweight and 86 (30.3%) obese women, $p < 0.01$ (Figure 2).

Term deliveries accounted for 915 deliveries (91.2%). Due to the small number of preterm deliveries (n=78) and post-term deliveries (n=16), statistical analysis was limited.

The heaviest babies were born in the category of obese women (Figure 3). There were 22 macrosomic offspring of which 20 (90.9%) were born to overweight and obese mothers. Among term offspring, 51% were males and 49% were females with no significant overall difference in the birthweights between them. The median(IQR) birthweights of males were 3160g(2900, 3500) and of females were 3060g (2770, 3285).

Table 1: Characteristics of study population

Characteristics	Median interquartile range (IQR)
Maternal Age	25 (14,44)
Gravidity	2 (1,8)
Parity	1 (0,6)
Body Mass Index(BMI) (kg/m^2)	26.2 (14.7, 57.7)
BMI categories(kg/m^2)	Frequency (%)
Underweight (< 18.5)	31 (3.1)
Normal (18.5 - 24.9)	394 (39.7)
Overweight (25.0 - 29.9)	284 (28.6)
Obese (> 30)	284 (28.6)
Class I (30 - 34.9)	163 (16.4)
Class II (35 - 39.9)	81 (8.2)
Class III (> 40)	40 (4.0)
HIV status	
Infected	422 (42.5)
Non-infected	571 (57.5)
	Median
Gestational age at booking (weeks)	17+4
Gestation of dating ultrasound(weeks)	n (%)
First semester (< 14+0)	306 (30.8)
Second semester (14+1 - 24+0)	687 (69.2)

Figure 1: Prevalence of comorbidities in study cohort across BMI categories

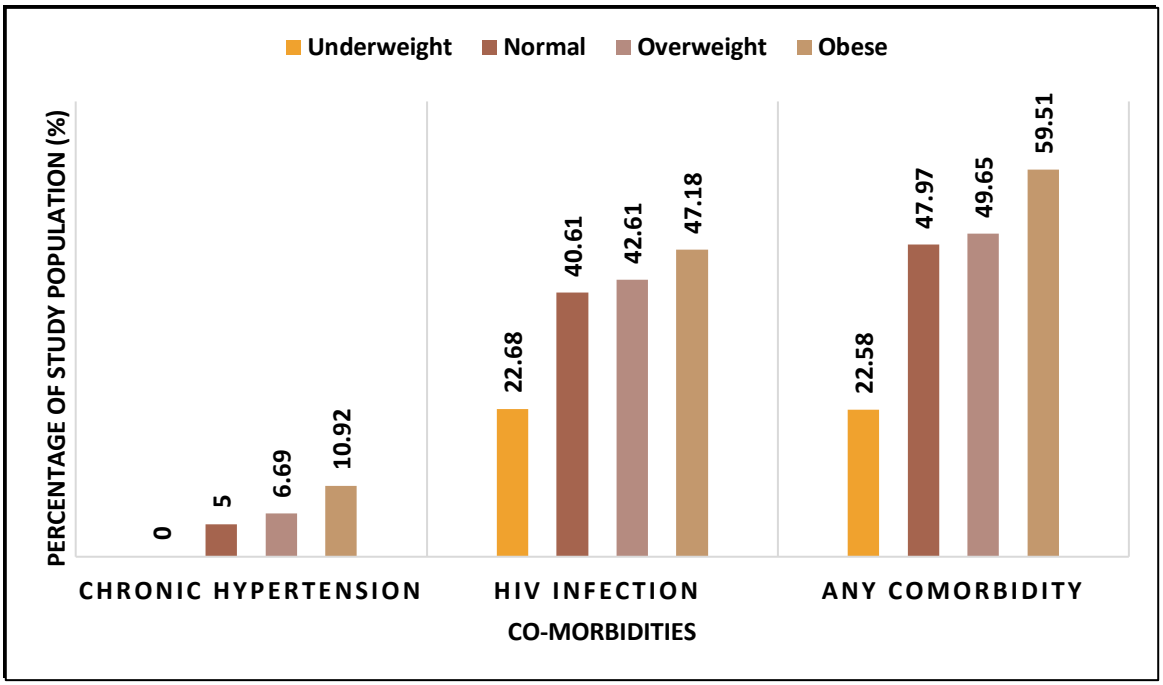


Figure 2. Rates and modes of delivery of study cohort across BMI categories

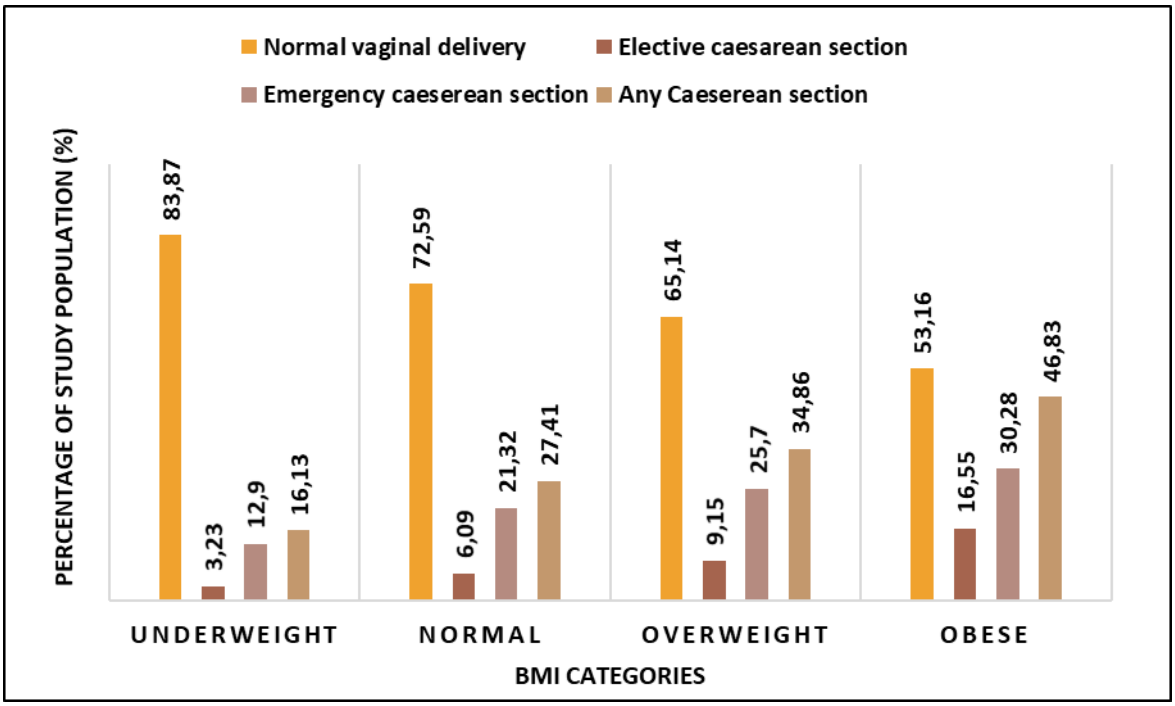
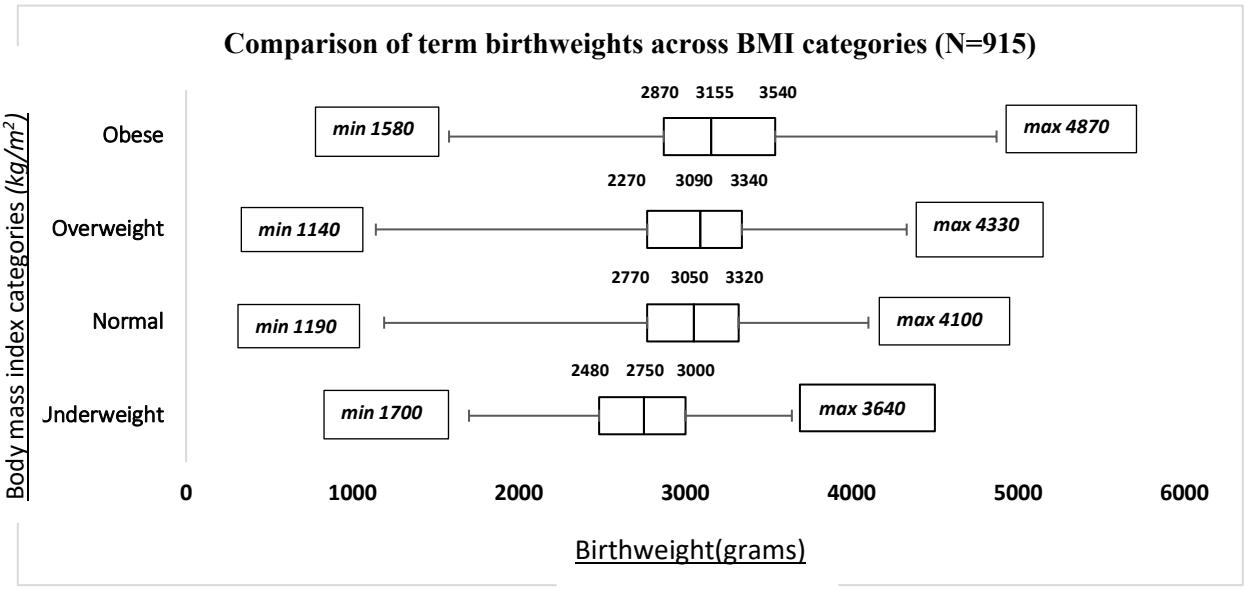


Figure 3. Box and whisker plot indicating median values, IQR and range of birthweight of term offspring for each category of maternal BMI .



Chapter 5

5.1. Discussion

The HIV-infection prevalence in our cohort was 42.5%, similar to the prevalence reported for KZN by the 2017 National Antenatal Sentinel HIV survey of 41.1%[27]. This provides reassurance that our cohort is likely representative of the wider population of pregnant women in KZN.

In our cohort of 993 women, 28.6% were overweight and a further 28.6% were obese. These prevalences are much lower than those reported in 2 other South African studies in which Basu reported prevalences of 37% overweight and 44% obese and Madlala reported 24.6% overweight and 44.4% obese in their cohorts[17,28]. The differences in the prevalences may be attributable to several factors; different geographic study locations in SA with ethnically diverse populations (cohorts for the studies by Basu[17] and Madlala[28] were from Gauteng and the Western Cape provinces respectively versus our study in KZN) and different levels of hospitals managing patients at various levels of risk with obesity being one such risk factor (Basu's study was at a tertiary hospital and Madlala's study was at a community health centre versus our study conducted at a district/regional hospital). Additionally, in all 3 studies the BMI was calculated at the booking visit, of note all patients in our cohort booked before 24weeks of pregnancy with a median gestational age at booking of 17weeks and 5 days while the median gestational age at booking in the study of Basu was 28 weeks (IQR, 23–32 weeks) and in excess of 15% of the cohort in the study by Madlala booked after 24weeks of pregnancy. Our study demonstrated an earlier gestational age at booking which is in keeping with previous reports showing booking before 20weeks of pregnancy in 73,2% of women in KZN and 76.1% of women in the iLembe district[29]. As the gestational age advances the gestational weight gain of pregnancy impacts on the BMI calculated hence this may be reflected in the higher prevalences of overweight and obese women in the studies by Basu and Madlala. This is supported by an African systematic review and meta-analysis where it demonstrated prevalences of obesity using the early booking BMI of 6.5 – 44.0% while third trimester reports indicated prevalences between 14.0 and 50.7%[30].

In our study overweight and obese women experienced chronic hypertension, HIV-infection or any comorbidity more than women of normal BMI, $p < 0.01$. A recent study analysing data from 13 countries in Africa reported an aOR of hypertension in the presence of obesity among non-pregnant women of 2.1 (1.8–2.4) suggesting that obesity and hypertension are 2 of the most important risk factors for morbidity and mortality in Africa[31].This supports our findings of the association of obesity with chronic hypertension. The prevalence of HIV-infection increased with increasing maternal BMI demonstrating the highest prevalence of 47.2% among obese women in our cohort. Other local studies have demonstrated similar findings citing possible reasons for this association; as attempts by women to defy the stigma of leanness being associated with HIV/AIDS and cultural beliefs that rounder physique is positively connotated with 'good' health[3,4,6]. The association between any comorbidity and obesity is of particular concern in SA as medical and surgical conditions are a major underlying cause of maternal mortality and have superceded hypertensive disorders of pregnancy and obstetric haemorrhage to become the leading direct cause of maternal mortality[32.] This highlights the rise of non-communicable diseases as a potentially modifiable contributory factor in maternal mortality.

Our cohort demonstrated increasing offspring birthweight with increasing maternal BMI ($p < 0.01$) with the heaviest babies born to the heaviest women and 91% of macrosomic babies born to women in the overweight and obese BMI categories. Maternal obesity is associated with epigenetic remodelling with alterations in DNA methylation in sites linked with offspring adiposity hence higher maternal BMI has an effect on offspring metabolic outcomes and increases the risk for excessive adipose accumulation, larger for gestational age and obesity during childhood and adolescence[23-25]. This poses a further public health concern as one would expect that paralleling the growing population of obese children and adolescents is a greater burden of non-communicable diseases.

The rates of both elective and emergency caesarean deliveries increased as the maternal BMI increased, $p < 0.01$. The rates of elective and emergency caesarean deliveries were highest amongst obese women with approximately one-third of women in this BMI category having undergone an emergency caesarean delivery and close to half of them having undergone any caesarean delivery. The association

of higher caesarean delivery with increasing BMI has also been shown in several other local and international studies[8,9,17,33] and may be explained by increased myometrial lipid deposition resulting in inefficient contractions, increased soft tissue narrowing of the birth canal and a macrosomic passenger[8,33-35]. High maternal weight also poses challenges to intrapartum fetal monitoring, with loss of contact from external placement of transducers making cardiotocographic monitoring particularly challenging. Similarly, internal monitoring with fetal scalp electrode placement and intrauterine pressure catheters are avoided in the setting of high HIV-infection prevalence to minimize the risk of vertical transmission of infection to the fetus[36]. This poses the risk of suboptimal fetal monitoring and increased operative risks to the mother, with mortality 3-fold higher in comparison to vaginal delivery[37]. The Saving Mothers and Babies report (2017-2019) noted a marked overall increase in caesarean delivery rates (28.1%) in state-subsidized facilities in SA which is comparable to the rate of 34.7% in our cohort, at a regional level setting[37]. Macrosomic offspring were most prevalent amongst the overweight and obese BMI groups, similar findings suggest an increased risk of caesarean delivery due to cephalon-pelvic disproportion and obstructed labour[8,33-35]. In SA, the burden of high BMI and increasing rates of caesarean delivery remain unabated and with it comes further risks of repeat operative delivery with its attendant complications. This poses new challenges for subsequent pregnancies with increased BMI and a previous caesarean section. These include obstetric surgical related risks of difficult repeat caesarean section due to loss of anatomical landmarks and arduous abdominal entry with greater risk of postpartum haemorrhage .This is further compounded by anaesthetic related risks of fluid retention and stasis, excessive secretions in lungs and poor ambulation peri- and post-operatively increasing thromboembolic risk[21,22]. Other postoperative complications include; prolonged hospital stay due to increased risk of local wound sepsis due to warmth and moisture beneath the pannus and hypostatic pneumonia[22].

5.2. Study strengths and limitations

The strengths of this study are that all women had early (≤24 weeks gestational age) obstetric ultrasound examinations performed by a single accredited sonographer, in

keeping with high booking rates (76.1%) before 20 weeks of gestation in the iLembe district[29]. There was good representation of diverse socioeconomic backgrounds with a large sample size. This is the first study performed assessing the pregnancy characteristics and outcomes across all BMI categories. Due to the retrospective nature of the study, the BMI calculated at first antenatal visit was used in the analysis and future research should focus on obtaining pre-pregnancy BMI and determining the gestational weight-gain in pregnancy and outcomes.

5.3. Conclusions and recommendations

Overweight and obese pregnant women showed a higher prevalence of HIV-infection and chronic hypertension. Similarly, they also had a higher prevalence of caesarean delivery and larger offspring compared to their normal and underweight counterparts. This highlights the growing burden of overweight and obesity as a non-communicable disease and its future health implications for reproductive-aged women. Our recommendation is that public health programs and initiatives should be directed towards; identifying at-risk reproductive-aged women, enrolment in pre-pregnancy clinics, support with sustainable weight loss, exercise and dietary programs, ongoing community education of healthy food choices and active lifestyles, encouraging planned pregnancies, long-term non-hormonal contraception promotion during weight optimisation and destigmatisation of chronic diseases like HIV/AIDS.

Appendices:

1. Data collection sheet
2. BREC approval and recertification
3. Hospital approval for collection of data from Stanger Regional Hospital
4. References

PT NO.	Clinic	P	G	Age	H	W	BMI	BMI category	HIV 1 2	ARV 1 2	Comorbidity	Smoker 1 2	Drugs 1 2	Alcohol 1 2	Date EUS	CRL	BPD	HC	AC	FL	DOB	Gestational age at birth	Delivery 1 2 3	ELCS	Indication	EMCS	Indication	BW	Gender 1 2

Data Collection Sheet

PT No. : Patient number

P: Parity
G: Gravidity

H: Height in metres
W: Weight in kilograms

BMI : Body mass Index : Weight/ (Height^2)
BMI category : WHO Classification

Comorbidities
1Hypertension
2 Diabetes Mellitus
3 Anaemia
4 Other: Epilepsy/Medical condition

Smoker :
1 User
2 Non user

Drugs :
1 User
2 Non user
Alcohol:
1 User
2 Non user

HIV : Human immundeficiency virus
1 Positive
2 Negative

ARV : Antiretroviral Drugs
1 User
2 Non user
3 Not applicable

Date EUS : Date early ultrasound (dd/mm/yyyy)

CRL : Crown rump length in millimetres
BPD: Biparietal diameter in millimetres
HC: Head circumference in millimetres
AC Abdominal circumference in millimetres
FL: Femur length in millimetres

DOB: Date of birth

Gestational age at birth : in days

Delivery
1 Normal vaginal delivery
2 Emergency caesarean section
3 Elective caesarean section

ELCS : Elective caesarean section
EMCS : Emergency caesarean section

BW: Birthweight in grams

Gender:
1 Male
2 Female

UNIVERSITY OF
KWAZULU-NATAL
INYUVESI
YAKWAZULU-NATALI
RESEARCH OFFICE
Biomedical Research Ethics Administration
Westville Campus, Govan Mbeki Building
Private Bag X 54001
Durban
4000
KwaZulu-Natal, SOUTH AFRICA
Tel: 27 31 2604769 - Fax: 27 31 2604609
Email: BREC@ukzn.ac.za
Website: http://research.ukzn.ac.za/Research-Ethics/Biomedical-Research-Ethics.aspx

10 December 2018

Dr P Sewmungal (218083695)
School of Clinical Medicine
College of Health Sciences
payalsewmungal@gmail.com

Dear Dr Sewmungal

Protocol: A retrospective South African study of patient characteristics and pregnancy outcomes in a cohort of women across various Body Mass Index categories.
Degree: MMed
BREC REF: BE669/18

PROVISIONAL APPROVAL

A sub-committee of the Biomedical Research Ethics Committee has considered your application received on 08 November 2018.

The study is given **PROVISIONAL APPROVAL** subject to the submission of:

- Gatekeeper permissions (Site and Department of Health).

Please email your response to brec@ukzn.ac.za .
All changes to the text must be highlighted and the relevant pages of the research application form resubmitted.
Only one copy of the responses and amended pages needs to be submitted.
Only when full ethical approval is given, may the study begin. **Full ethics approval has not been given at this stage.**
PLEASE NOTE: Provisional approval is valid for 6 months only - should we not hear from you during this time - the study will be closed and reapplication will need to be made.
Your acceptance of this approval denotes your compliance with South African National Research Ethics Guidelines (2015), South African National Good Clinical Practice Guidelines (2006) (if applicable) and with UKZN BREC ethics requirements as contained in the UKZN BREC Terms of Reference and Standard Operating Procedures, all available at http://research.ukzn.ac.za/Research-Ethics/Biomedical-Research-Ethics.aspx.
BREC is registered with the South African National Health Research Ethics Council (REC-290408-009). BREC has US Office for Human Research Protections (OHRP) Federal-wide Assurance (FWA 678).

Yours sincerely

Prof V Rambiritch
Chair: Biomedical Research Ethics Committee

Supervisor: Budhrams@icloud.com
Postgrad admin: Ms AL Molemong

UNIVERSITY OF KWAZULU-NATAL
INYUVESI YAKWAZULU-NATALI

26 April 2019

Dr P Sewmungal (218083695)
School of Clinical Medicine
College of Health Sciences
payalsewmungal@gmail.com

Dear Dr Sewmungal

Protocol: A retrospective South African study of patient characteristics and pregnancy outcomes in a cohort of women across various Body Mass Index categories.
Degree: MMed **BREC REF: BE669/18**

EXPEDITED APPLICATION: APPROVAL LETTER

A sub-committee of the Biomedical Research Ethics Committee has considered and noted your application received 08 November 2018.

The study was provisionally approved pending appropriate responses to queries raised. Your response received on 15 April 2019 to BREC correspondence dated 10 December 2018 has been noted by a sub-committee of the Biomedical Research Ethics Committee. The conditions have been met and the study is given **full ethics approval** and may begin as from 26 April 2019. Please ensure that site permissions are obtained and forwarded to BREC for approval before commencing research at a site.

This approval is valid for one year from **26 April 2019.** To ensure uninterrupted approval of this study beyond the approval expiry date, an application for recertification must be submitted to BREC on the appropriate BREC form 2-3 months before the expiry date.

Any amendments to this study, unless urgently required to ensure safety of participants, must be approved by BREC prior to implementation.

Your acceptance of this approval denotes your compliance with South African National Research Ethics Guidelines (2015), South African National Good Clinical Practice Guidelines (2006) (if applicable) and with UKZN BREC ethics requirements as contained in the UKZN BREC Terms of Reference and Standard Operating Procedures, all available at http://research.ukzn.ac.za/Research-Ethics/Biomedical-Research-Ethics.aspx.

BREC is registered with the South African National Health Research Ethics Council (REC-290408-009). BREC has US Office for Human Research Protections (OHRP) Federal-wide Assurance (FWA 678).

The sub-committee's decision will be **noted** by a full Committee at its next meeting taking place on **14 May 2019.**

We wish you well with this study. We would appreciate receiving copies of all publications arising out of this study.

Yours sincerely

Professor V Rambiritch
Chair: Biomedical Research Ethics Committee

Supervisor: Budhrams@icloud.com Postgrad admin: Ms AL Molemong

UNIVERSITY OF KWAZULU-NATAL
INYUVESI YAKWAZULU-NATALI

09 April 2020

Dr P Sewmungal (218083695)
School of Clinical Medicine
College of Health Sciences
payalsewmungal@gmail.com

Dear Dr Sewmungal

Protocol: A retrospective South African study of patient characteristics and pregnancy outcomes in a cohort of women across various Body Mass Index categories.
Degree: MMed
BREC REF: BE669/18

RECERTIFICATION APPLICATION APPROVAL NOTICE

Approved:	26 April 2020
Expiration of Ethical Approval:	25 April 2021

I wish to advise you that your application for Recertification received on 06 April 2020 for the above protocol has been **noted and approved** by a sub-committee of the Biomedical Research Ethics Committee (BREC) for another approval period. The start and end dates of this period are indicated above.

If any modifications or adverse events occur in the project before your next scheduled review, you must submit them to BREC for review. Except in emergency situations, no change to the protocol may be implemented until you have received written BREC approval for the change.

Note to PI: It is noted that the planned number of cases (1000) has been exceeded. This is a protocol violation and can be condoned. However any further changes to this study must be preceded by an amendment application before being implemented.

The committee will be notified of the above approval at its next meeting to be held on 12 May 2020.

Yours sincerely

Ms A Marimuthu
(for) Prof D Wassenaar
Chair: Biomedical Research Ethics Committee

cc supervisor: yasmin.goga@gmail.com cc postgraduate administrator: nalal@ukzn.ac.za

UNIVERSITY OF KWAZULU-NATAL
INYUVESI YAKWAZULU-NATALI

13 April 2021

Dr P Sewmungal (218083695)
School of Clinical Medicine
College of Health Sciences
payalsewmungal@gmail.com

Dear Dr Sewmungal

Protocol: A retrospective South African study of patient characteristics and pregnancy outcomes in a cohort of women across various Body Mass Index categories.
Degree: MMed
BREC REF: BE669/18

RECERTIFICATION APPLICATION APPROVAL NOTICE

Approved:	26 April 2021
Expiration of Ethical Approval:	25 April 2022

I wish to advise you that your application for Recertification received on 08 April 2021 for the above protocol has been **noted and approved** by a sub-committee of the Biomedical Research Ethics Committee (BREC) for another approval period. The start and end dates of this period are indicated above.

If any modifications or adverse events occur in the project before your next scheduled review, you must submit them to BREC for review. Except in emergency situations, no change to the protocol may be implemented until you have received written BREC approval for the change.

The committee will be notified of the above approval at its next meeting to be held on 11 May 2021.

Yours sincerely

Ms A Marimuthu
(for) Prof D Wassenaar
Chair: Biomedical Research Ethics Committee

health
Department:
Health
PROVINCE OF KWAZULU-NATAL

Physical Address: 330 Langalibalele Street, Pietermaritzburg
Postal Address: Private Bag X9051
Tel: 033 395 2805/ 3189/ 3123 Fax: 033 394 3782
Email:
www.kznhealth.gov.za

DIRECTORATE:
Health Research & Knowledge Management

Ref: KZ_201901_014

Dear Dr P Sewmungal
(UKZN)

Subject: Approval of a Research Proposal:

1. The research proposal titled **'A retrospective South African study of patient characteristics and pregnancy outcomes in a cohort of women across various Body Mass Index categories'** was reviewed by the KwaZulu-Natal Department of Health.

   The proposal is hereby **approved** for research to be undertaken at Stanger hospital.

2. You are requested to take note of the following:

   a. *Kindly liaise with the facility manager BEFORE your research begins in order to ensure that conditions in the facility are conducive to the conduct of your research. These include, but are not limited to, an assurance that the numbers of patients attending the facility are sufficient to support your sample size requirements, and that the space and physical infrastructure of the facility can accommodate the research team and any additional equipment required for the research.*
   b. *Please ensure that you provide your letter of ethics re-certification to this unit, when the current approval expires.*
   c. *Provide an interim progress report and final report (electronic and hard copies) when your research is complete.*

3. Your final report must be posted to **HEALTH RESEARCH AND KNOWLEDGE MANAGEMENT, 10-102, PRIVATE BAG X9051, PIETERMARITZBURG, 3200** and e-mail an electronic copy to hrkm@kznhealth.gov.za

For any additional information please contact Ms G Khumalo on 033-395 3189.

Yours Sincerely

Cerate.

Dr E Lutge
Chairperson, Health Research Committee
Date: 05/04/19.

health
Department:
Health
PROVINCE OF KWAZULU-NATAL

NAME OF INSTITUTION/DISTRICT/COMPONENT
Postal Address: Private Bag x10609, Stanger 4450

Tel: 0324376015 Fax. 0867567812
Email.gustavo.lopez@kznhealth.gov.za
www.kznhealth.gov.za

OFFICE OF THE SENIOR MANAGER: MEDICAL SERVICES

Enquiries: Dr. G. Lopez
EXT: 6015
DATE: 16/04/2019

Dr P Sewmungal

RE: PERMISSION TO CONDUCT RESEARCH AT STANGER HOSPITAL.

Dear Dr Seumungal

I have pleasure in informing you that permission has been granted to you by Stanger Hospital to conduct research on: A retrospective South African study of patient characteristics and pregnancy outcomes in a cohort of women across various Body Mass Index categories.

Please note the following:

1. Please ensure that you adhere to all policies, procedures, protocols and guidelines of the Department of Health with regards to this research.
2. This research will only commence once this office has received confirmation from the Provincial Health Research Committee in the KZN Department of Health.
3. Please ensure this office is informed before you commence your research.
4. Stanger Hospital will not provide any resources for this research.
5. You will be expected to provide feedback on your findings to Stanger Hospital.

Thanking you;

Senior Manager: Medical Services
Stanger Hospital

APPENDIX 9

PERMISSION TO CONDUCT A RESEARCH STUDY/TRIAL

This must be completed and submitted to the Medical Superintendent/s / Hospital Manager for signature.

For King Edward VIII Hospital (KEH) and Inkosi Albert Luthuli Central Hospital (IALCH) studies please submit together with the following:

i) Two copies of the final, approved protocol
ii) Letter giving provisional ethical approval
iii) Details of other research presently being performed by yourself (individually or as a collaborator)
iv) Details of any financial or human resource implications to King Edward VIII Hospital
v) If a clinical trial, please produce proof of payment or intention thereof to KEH

Once the document has been signed it should be returned to this office so that full ethical approval can be granted.

To: Hospital Manager

PROTOCOL

Permission is requested to conduct the above research study at the hospital/s indicated below:

Site 1 address:

Stanger Hospital
P Sewmungal
Kwadukuza

Investigator/s:
Principal: Dr

Co-investigator: -

Signature of Hospital Manager :

Date: ~~26/3/19~~ 16/04/19

Site 2 address: Investigator/s

_____ Principal: _____
_____ Co-investigator: _____
_____ Co-Investigator: _____

Signature of Hospital Manager :

_____ Date: _____

NB: Hospital Manager/s to send a copy of this document to Natalia.

Key references:

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