Gestational Diabetes Mellitus (GDM): Challenges of Adherence to Anti-Diabetic Therapy and Perinatal Outcomes in Pregnant Women with GDM. A Proposal for Research

Doreen Mukona[1], Stephen Peter Munjanja[2], Mathilda Zvinavashe[3], Babill Stray-Pederson[4]

[1,3]*University of Zimbabwe College of Health Sciences, Department of Nursing Science*
[2]*University of Zimbabwe College of Health Sciences, Department of Obstetrics and Gynecology*
[4]*University of Oslo, Institute of Clinical Medicine, Division of Women and Children, Rikshospitalet, Oslo University Hospital, N-0027 Oslo, Norway*

Abstract : *Diabetes is a global public health challenge with negative impacts on all countries. Zimbabwe, with a prevalence of diabetes of 9,7% is ranked 4th among African countries with the highest prevalence of diabetes. Prevalence of GDM, which is hyperglycaemia first detected during pregnancy, closely follows underlying prevalence of type 2 diabetes mellitus in a population. Anti-diabetic therapy includes diet exercise and medications. Adherence to long term therapies is generally problematic. GDM if left untreated, causes a number of adverse perinatal outcomes including preeclampsia, preterm labour, still births, neonatal hypoglycaemia, hyperbilirubinemia and neonatal deaths. The purpose of the study will be to examine challenges of adherence to anti-diabetic therapy and perinatal outcomes in pregnant women with GDM. This study will utilise a cohort design (quantitative) with pregnant women with GDM and phenomenological (qualitative) design with health care professionals caring for pregnant women with GDM. All eligible women presenting at the study sites will be recruited into the study .The study will be carried out at three central hospitals in Zimbabwe. Ethical clearance will be obtained from respective institutional review boards and the Medical Research Council of Zimbabwe. Participants will give informed consent prior to participation in the study. Privacy and confidentiality will be observed before, during and after the study. Data will be collected through structured interviews with pregnant women, key informant interviews with health care givers, focus group discussions (FGD) with pregnant women and review of records of women. Pill counts will be done to measure adherence to medication while a wearable device, Pulsense PS 100R will be used on the pregnant women to measure physical activity, caloric expenditure, sleep patterns and heart rate. Results will be presented in tables, pie charts and graphs. Data will be analysed using SPSS version 20. Descriptive statistics will be used to analyse data on demographics, rates of adherence to anti-diabetic therapy and perinatal outcomes. Inferential statistics will be used to analyse data on the relationship between adherence and perinatal outcomes. Qualitative data will be transcribed and themes will be identified. Appropriate recommendations and conclusions will be made from findings.*
Keywords: *adherence, diabetes mellitus, gestational, perinatal outcomes*

I. Introduction

Diabetic is now a global public health challenge with serious negative impacts on all countries [1]. Diabetes mellitus is one of the non-communicable diseases which are predominant causes of mortality in Africa although infectious diseases outnumber diabetes and other non-communicable disease (NCDS) as the predominant cause of motility in the region [2]. However, it is projected that within the two coming decades NCDs would have overtaken infectious diseases as the predominant cause of mortality in the region [2].The anticipated increase in the prevalence of diabetes in Africa will be due to development, longer life expectancy and the likely progression of people at high risk for the development of type 2 diabetes. This comprises a sizable portion of the population and includes those with impaired glucose (IGT), the prevalence of which was 7.3% among 20-79 year olds in 2013. However, there are no adequate measures in Africa to stop progression to diabetes for people at high risk in view of the low level of development [3]. In terms of numbers of cases of diabetes, there were 600 668 people with diabetes in Zimbabwe and it ranked 8th in Africa in 2013 Urbanization in Africa, has largely contributed to the evolving problem of chronic diseases, mainly diabetes mellitus [4].This rise will most likely result in an increase in GDM in Africa, though the prevalence of GDM is relatively unknown [5].The incidence of GDM reflects the incidence of type 2 diabetes mellitus in the background population [6]. The prevalence of GDM ranges from 2%-4% in pregnancy worldwide [13]. Furthermore, there

will be more women with diabetes than men and a considerable raise in the burden of GDM is anticipated especially in less affluent countries [7].

GDM is a metabolic disorder characterised by glucose intolerance which is first recognised during pregnancy. Insulin sensitivity in pregnant women is significantly reduced during late gestation putting the pregnant women at risk of hyperglycemia [8].The high levels of several diabetogenic hormones (placental growth hormone (GH), placental lactogen, and circulating insulin-like growth factor-I (IGF-I) lead to a state of insulin resistance during pregnancy and pronounced physiological decrease in peripheral insulin sensitivity occurs as pregnancy proceeds [9].

GDM can negatively affect pregnancy, resulting in adverse perinatal outcomes such as hypoglycaemia , hyperbilirubinemia, shoulder dystocia, macrosomia, birth trauma and high rates of caesarean section and still birth [10].The three cornerstones of diabetes management are diet, physical activity and medication, if necessary [11]. Nutritional therapy is an integral component in the prevention and management of diabetes mellitus and has been shown to result in sustained improvements in glycated haemoglobin (HbA1C) in clinical trials [12]. Treatment of GDM, as revealed by the Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS), improves pregnancy outcome [13].The focus of clinical interventions is maintenance of euglycemia with a combination of diet and exercise then introduction of insulin when diet and exercise fail [14].Adherence in chronic disorders is the extent to which a person follows recommendations for therapy such as taking medication, following diet, and/or executing lifestyle changes as advised by a health care provider [15]. Adherence to healthy eating and exercise to maintain healthy weight during pregnancy remains problematic [16]. It is important to identify and address individual psychological aspects and the impact that they may have on successful behavioural change in pregnant women [17]. Women with GDM can give birth to healthy neonates provided their blood glucose levels are well controlled with a diabetic diet, exercise and and appropriate body weight [10]. Management of pregnant women with GDM therefore is a challenge that health care professionals face daily because of the complexity of the therapeutic regimen for GDM [18]. Management of GDM is a perfect window of opportunity for the prevention of diabetes mellitus in two generations, and awareness of the condition among antenatal women will translate into prevention and early diagnosis of the disease [19].   The purpose of this study, therefore, will be to examine adherence to anti-diabetic therapy, challenges and perinatal outcomes in pregnant women with GDM at central hospitals in Harare and Chitungwiza, Zimbabwe.

II.   Materials And Methods

2.1 Design
The study will be concluded in 2 phases namely qualitative and quantitative phases. The quantitative phase will be conducted on a cohort of 157 pregnant women with a confirmed diagnosis of GDM. The qualitative phase will be conducted using a phenomenological design with 15 health care professionals involved in the care of women with GDM and 56 pregnant women. A phenomenological design helps to understand the essence of a phenomenon from the perspective of the people experiencing it [20]. In this study the phenomenon of interest is GDM and the people experiencing it are the pregnant women with GDM and health care professionals caring for these women. A stratified purposive sample of 15 health care professionals, 5 from each of the maternity hospitals will be recruited into the study. The 5 professionals will comprise an obstetrician, a physician, a midwife, a physiotherapist and a dietician. Health care worker will give information on current management of GDM at the hospitals, the burden of the disease and challenges in the management of GDM and possible solutions to the problem from a health care worker perspective. Eight FGDs will be conducted with pregnant women. Four of the FGDs will be conducted at Harare Maternity hospital and 2 will be conducted at Mbuya Nehanda and 2 at Chitungwiza. This is because Harare maternity is the main referral hospital for diabetes in pregnancies and majority cases are managed there. The four FGDs at Harare maternity hospital will comprise 7 pregnant women each. A total of 56 women from the 157 women will participate in FGDs. It is hoped that qualitative data will be obtained from the women about the burden of GDM, the challenges of adherence to anti-diabetic therapy and the possible solutions from patients' perspective.

2.2 Setting
The study will be conducted at 3 central hospitals in Zimbabwe. All women presenting at the sites with GDM during the period of data collection will be eligible for recruitment into the study. Included in the study will be pregnant women with a confirmed diagnosis of GDM. Excluded will be the very ill, institutionalised and mentally unstable women.

2.3 Variables

The variables under study will be demographics, adherence to anti-diabetic therapy, factors influencing adherence to anti-diabetic therapy, perinatal outcomes and the relationship between adherence to anti-diabetic therapy and perinatal outcomes.

2.4 Instruments

A structured questionnaire with sections on demographic data, past and current pregnancy history and adherence to medication, diet and physical activity and perinatal outcomes will be used to collect quantitative data from the pregnant women during the quantitative phase. A data sheet will be developed from the questionnaire that will be a coded and shorter version of the questionnaire. It will be used for data collection and for data entry into SPSS for analysis. Scoring will be done on the sections of adherence to medications, adherence to diet and adherence to physical activity. A composite sore of adherence to diet, medications and physical activity will be calculated by adding the three scores. The higher the score on adherence, the higher the level of adherence. Adverse perinatal outcomes will also be scored. The perfect score on perinatal outcomes will be zero. The higher the score, the more the perinatal outcomes and the poorer the perinatal outcomes. Perinatal outcomes will include caesarean delivery, preeclampsia, and neonatal hypoglycaemia, preterm labour and prematurity and neonatal death. Records reviews will also be done on antenatal records to get information on weights, blood pressure, any other comorbidities, blood sugar control and perinatal outcomes. Pill counts will be done to objectively measure adherence to medications. These will be done each time a participant comes for review and regular ante-natal care. Participants will be instructed, on the initial visit, to bring their medication in their original packets each time they come to the ante-natal clinic. The tablets will be physically counted by the research staff to check if there have been any missed doses. These will compliment self-reports which tend to overestimate adherence as participants are likely to give socially desirable responses. However with pill counts, participants might throw away medications not consumed and this might still overestimate adherence. The important of adherence to medications and honesty when one has not taken their drugs will be stressed on recruitment into the study.

A wearable device, Pulsense PS 100[R] will be used to objectively measure calories burnt during activity, physical activity, sleep patterns and heart rate. The device will be used on some participants to complement subjective data obtained by self-reports. Key informant interviews following a semi structured questionnaire with obstetricians, midwives, physiotherapists and dieticians will be conducted during the qualitative phase to get the view on challenges in the management of GDM. FGDs using a semi structured questionnaire will be conducted with pregnant women will be conducted to get qualitative data on challenges of adherence to anti-diabetic therapy.

2.5 Procedures

Participants will be recruited into the study at first contact with the researcher, Upon entry into the study there will be measurement of glycated haemoglobin, measurement of vital signs including blood pressure, blood sugar, weight, height, urinalysis, interviews on demographic data, past pregnancy history and current health status, key informant interviews with health care providers and recording of data. Participants will be required to come fortnightly for follow up visit and this coincides with their visit for regular maternity care. During follow up of participants, interviews on adherence to diet, physical activity and medications will be done while key informant interviews with health care providers will be continuing. There will be ongoing measurement of vital signs including blood pressure, blood sugar, weight, height, urinalysis and pill counts and objective measurement of adherence to diet and physical active using Pulsense PS-100[R]. Participants will be given education on use and care of the Pulsense PS -100[R]. The importance of wearing it continuously for a full week without removing it and bringing it back to the site for data retrieval will be stressed. There will be routine fetal monitoring, monitoring for any maternal morbidities and perinatal outcomes, ongoing recording, cleaning and analysing of data. FGDs will also be conducted.

Participants will exit the study for six weeks after delivery. There will be measurement of vital signs including blood pressure, blood sugar, weight, height and urinalysis. A summary of blood sugar control, adherence, and perinatal outcomes will be compiled. There will be final data entry and preparation for final analysis.

2.6 Pilot study

A pilot study with the structured questionnaire will be done on 10 pregnant women with GDM to train the research assistants, to evaluate how data will be analysed for possible problems, and to clarify what financial and human resources will be needed. It will also be done with the semi structured interview for key informant interviews with 3 health care professionals, one from each study site.

2.7 Ethical considerations

The three u universally applicable principles of research, namely, respect for person, beneficence and justice will be observed during and after the study. All study participants will be required to give voluntary and informed consent. Participants will be informed of the absence of direct benefits to them as a result of participation in the study. There will be recognition of patient's time, however, and it will be reasonably compensated to avoid undue inducements. Participant will each receive five United States Dollars as compensation for their time for interviews and procedures. Participants will be informed that they are free to withdraw from the study at any point without attracting any penalties from the health care workers. Participants will also be advised that they will be free to withhold any information they do not feel comfortable divulging. There will be assurance of confidentiality and privacy. Interviews and procedures will be done in a private room and code numbers will be used for identification of participants rather than their names. All information obtained will be kept under lock and key and the researcher and assistant will have sole access to the information, only for the purposes of the research.

Permission to carry out the study will be sought from the respective study sites, the Joint Ethics Research Committee, the Medical Research Council of Zimbabwe and the central hospitals. Study participants, will still be entitled to recommended standards of care as offered at the central hospital during the time of the research. Research assistants to help with data collection will be trained to avoid undue discomfort on the participants, standardise the process of data collection and avoid bias. The researcher will be collaborating with other health care team members (midwives, obstetricians and gynaecologists) and will be under supervision by a consultant obstetrician and gynaecologist and a community nurse.

All women with GDM attending the 3 central hospitals during the time of data collection will be approached as potential study participants. Though they will not be any direct benefits for participating in the study, it is hoped that findings of the study will be utilised to improve the quality of care given to women with GDM thereby indirectly benefiting the participants, families and communities. The researcher or research assistant will introduce themselves to the prospective participant and explain in detail the purpose of data, benefits and risks involved in order to obtain informed consent. The process of obtaining informed consent from women with GDM and health care professionals will last 30 minutes to an hour. On agreeing, both the participant and the researcher will sign two identical copies of the informed consent form and both forms will be retained by the researcher. Interviews will be held in a private room. The researcher will be asking questions from the questionnaires and responses will be recorded on individual questionnaires. The interviews will last 30-40 minutes. At the end of the interview the participants will be thanked and be reminded that there will be routine follow up until 6 weeks after delivery. The participants will be advised that they will be routine checking of their cards and notes in order to extract data on blood pressure, blood glucose, medications being taken, comorbidities and perinatal outcomes. The participants therefore will be advised and encouraged to report for these reviews. The importance of delivering at the study site will be stressed to the participants.

All women with a confirmed diagnosis of GDM attending the central hospital in Harare during the period between December 2015 and November 2016 will be eligible to participate in the study if they do satisfy the inclusion criteria. If the required sample size of 157 participants will be reached before the proposed 12 months, data collection will be terminated at that point

2.8 Data analysis

Data from interview schedule will be extracted and entered into Epidata which is data management software. A code book will be generated automatically in Epidata as data is being entered. Data will be exported to the SPSS version 20 for analysis. Descriptive statistics (frequencies, means, standard deviation, minimum and maximum values, will be used to present data on demographic data, adherence to anti diabetic therapy and perinatal outcomes. Data will be presented in frequency tables, histograms and pie charts. Inferential statistics, Pearson's correlation and regression analysis will be used to analyse the relationship between adherence and perinatal outcomes. Chi square test will be done to test the hypothesis that adherence to anti-diabetic therapy reduces the incidence of perinatal outcomes in women with GDM. Recorded key informant interviews and FGDs will be transcribed by a professional transcriber into scripts. Thematic analysis of the scripts will be done.

III.   Results

Results will be discussed in terms of the variables under study and appropriate recommendations will be made. The results will be used to develop an adherence intervention to foster adherence to anti-diabetic therapy in pregnant women with diabetes in pregnancy. It is hoped that psychosocial assessment of women diagnosed with GDM will be done routinely at the health care centre to assess readiness to learn, challenges currently being faced by the women and to predict adherence to anti diabetic therapy. It is hoped that routine

assessment of adherence to anti-diabetic therapy and ongoing health education on management of GDM will be done to foster adherence to therapy

Acknowledgements

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