STUDY PROTOCOL

A Study Plan Outlining a Randomized Control Trial With Two Arms, Conducted in Parallel, to Investigate the Impact of a Health Education Intervention on the Utilization and Implementation of Insecticide-treated Nets Among Pregnant Women Attending Antenatal Clinics

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ABSTRACT

Introduction: Estimating the real extent of the health impact caused by malaria globally is essentially an educated estimation in the scientific realm. However, there is no denying that the most significant toll is observed in sub-Saharan Africa. **Methods:** This research will involve an intervention study utilizing a two-arm double-blind parallel randomized controlled trial, conducted in three stages. The initial stage will focus on creating a Health Belief Model (HBM) program. In the second stage, pregnant women will be enlisted, evaluated for baseline data, randomly assigned to two study arms, and monitored over a six-month period. The final phase will assess the influence of the intervention on the Health Belief Model (HBM) and share the results. Information will be gathered through a structured questionnaire incorporating validated instruments. The primary outcome will be the treatment effect assessed with the HBM Knowledge of malaria and ITNs use, attitude towards malaria and ITNs use, practices towards malaria and ITNs use, health seeking behaviour and health belief model factors, and data will be analyzed using SPSS, version 22 of the following analysis: Independent T-Test, Repeated Anova and (Gee) General Estimating Equation. **Discussion:** The research will add to the current understanding of care programs for pregnant women in hospitals in developing nations with limited existing literature. It will provide a broader perspective on the significance of measuring Health Belief Model (HBM) in intervention studies related to malaria and other infectious diseases in this specific context. **Trial Registration:** PACTR202312664285367
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INTRODUCTION

Malaria has impacted the lives of nearly 40% of the world's population, with pregnant women and children under the age of 5 being particularly vulnerable (1). Each year, approximately 10,000 women and 200,000 children lose their lives as a result of complications arising from malaria during pregnancy. Furthermore, on a global scale, Sub-Saharan Africa bears the brunt of malaria cases, accounting for approximately 85% of the total. In 2015, there were 214 million reported cases of malaria worldwide, resulting in 438,000 deaths (2). Notably, 20% of pregnant women who attend antenatal clinics test positive for the malaria parasite, specifically *Plasmodium falciparum*. Additionally, a significant 72% of pregnant women experience malaria infections during pregnancy, often unknowingly carrying the malaria parasite in their placenta. This factor makes them three times more susceptible to other acute illnesses (1-3).

The increase in 2020 was associated with disruption to services during the Covid-19 pandemic. Between 2019 and 2021, an estimated additional 13.4 million cases were attributed to disruptions during the Covid-19 pandemic (4-6). During childbirth, the risk of acquiring malaria increases through bites from infected mosquitoes (7). Africa has the highest global incidence of malaria, and it poses a significant public health challenge in Nigeria, contributing to higher cases and mortality rates compared to other diseases (8). Hospital review reports indicate that malaria is responsible for 30% of child

mortality, 60% of outpatient visits to health facilities, 11% of maternal mortality, and 25% of infant mortality (9).

Malaria is responsible for 20% of instances of stillbirths and 11% of maternal deaths, as well as contributing to spontaneous abortions, maternal anemia, placental pathologies, infant morbidity, and mortality. Additionally, it hinders the normal growth of the foetus in utero, resulting in decreased birth weight. Malaria is also associated with miscarriages and premature births, causing significant public health challenges for mothers, foetuses, and new-borns alike (10-11).

This trend is likely influenced by Nigeria's substantial population, with approximately 140 million people residing in areas where malaria transmission is prevalent (15). It is noteworthy that around 11% of maternal deaths in Nigeria are attributed to malaria (16). Various studies conducted by researchers have consistently shown elevated prevalence rates of malaria in pregnancy across different regions of Nigeria, ranging from 19.7% to 72.0% (17-19).

Previous research has underscored the effectiveness of health education interventions in improving malaria prevention practices, including ITN utilization, among pregnant women. For instance, (26) demonstrated that targeted health education significantly increased the uptake of ITNs among pregnant women in Ghana. Similarly, a systematic review by (28) highlighted the positive impact of health education interventions on malaria prevention behaviors among pregnant women in sub-Saharan Africa.

STUDY HYPOTESIS AND OBJECTIVE

The primary research inquiry of the study was as follows: "What are the effects of health education intervention on the practice of insecticide treated nets among pregnant women attending antenatal clinic in UNTH Enugu, Nigeria?" The hypothesis posited that pregnant women, when exposed to health education during their antenatal visits, would show significant enhancements in their knowledge, attitude, and practices related to the use of insecticide-treated nets, as well as improvements in health-seeking behavior outcomes. The specific objectives of the study include:

1. To describe and compare between the respondents in the intervention group and control group at baseline.
2. To determine the changes within intervention group from baseline to 3 and 6 months post intervention.
3. To compare the changes between intervention group and control group at 3 and 6 months post intervention.
4. To compare the difference between intervention group and control group at 3 and 6 months post intervention after controlling for covariates.

THE HEALTH BELIEVE MODEL

This research will follow the updated edition of the Health Belief Model to explore health behaviors and identify key health beliefs. While the Health Belief Model (HBM) framework has been extensively utilized and proven effective in predicting and influencing various health behaviors, its success has been moderate. Further experimental studies are required to examine the direct impact of manipulating Health Belief Model cognitions on behavior (20). Additional testing of interventions based on the Health Belief Model (HBM) is necessary. These tests should incorporate mediation analyses to investigate whether changes in Health Belief Model cognitions mediate the impact on behavior.

The Health Belief Model consists of six elements:

a.) Perceived susceptibility
b.) Perceived severity
c.) Perceived benefits
d.) Perceived barriers
e.) Cue to action
f.) Self-efficacy

CONCEPTUAL FRAMEWORK FOR THE STUDY

The conceptual framework for examining the effect of insecticide-treated nets (ITNs) practices on health education employs the Health Belief Model (HBM). A multidisciplinary approach, specifically task shifting, will be utilized wherein trained nurses will deliver care to pregnant women within the hospital setting. These nurses will undergo specific intervention training and operate under the guidance and supervision of a researcher to ensure the provision of effective follow-up and support to the pregnant women. Additionally, structured hospital-based questionnaires will be employed for follow-up assessments with the pregnant mothers. Central to this study is the implementation of a health education intervention module focused on malaria causation, preventive measures, various types of mosquito nets, advantages of ITNs, and the importance of consistent ITN usage. These educational components will serve as essential tools for data collection and analysis throughout the research process, aiding in understanding the impact of ITN practices on health education outcomes. The Health Belief Model HBM will influence the pregnant mother's health as shown in Figure 1 below.

The Health Belief Model (HBM) stands out as a widely utilized theory in the realm of health behavior (21). This

model encompasses six elements that anticipate health-related actions, comprising susceptibility to risk, severity of risk, perceived benefits of taking action, perceived barriers to action, self-efficacy, and cues prompting action. (22-23).

Originally designed for the adoption of preventive health behaviors in the United States, the Health Belief Model (HBM) has undergone successful adaptations to suit various cultural and topical contexts (24-25).

METHODS

Study setting
Ituku-Ozalla metropolis Nigeria is the study location were the study will be carried out, while recruiting patients will be from University of Nigeria Teaching Hospital (UNTH) Enugu.

Study design
This research plan involves a two-arm double-blind parallel randomized controlled trial with intervention, employing a blinded approach. The study will follow a three-step process outlined in Figure 1. The initial step focuses on providing health education interventions, covering topics such as the causes of malaria, methods of prevention, various types of mosquito nets, advantages of insecticide-treated nets (ITNs), and the significance of consistently using ITNs. This aims to inform participants about actions to prevent malaria and its management in the study area. The subsequent steps involve conducting pre-intervention and post-intervention assessments, as illustrated in Figure 1.

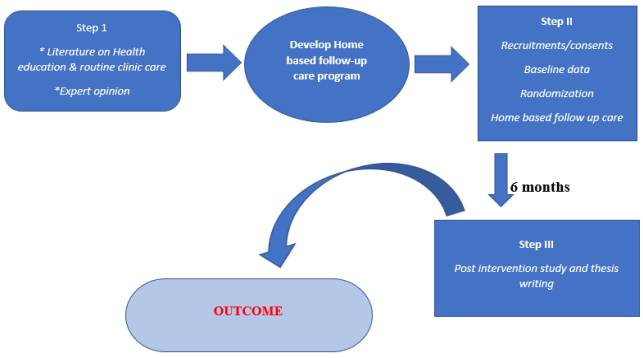

Figure 1: Research approach flowchart showing 3 phases of the research.

In Step two, informed consent from the recruited eligible patients will be obtained, followed by baseline data collection. Randomization into 2 arms of study will be carried out, which includes the following; intervention and control groups.

Subsequently, the intervention group will receive a structured hospital-based follow-up care framework and module, lasting for a period of 6 months. The third step involves conducting a post-intervention assessment, which will take place after the 6-month hospital-based follow-up care period.

Study population
The study population will be all pregnant mothers aged 18 years and above that enrolled antenatal clinic in UNTH, Enugu state, Nigeria.

Inclusion criteria
1. All pregnant women age 18 years and above, who registered for antenatal clinic in UNTH, Enugu State, Nigeria.
2. All pregnant women who are in their 1st and 2nd trimesters.
3. All pregnant women who has had past history of malaria.

Exclusion criteria
1. Pregnant women who are in their 3rd trimester (reasons: pregnant women in 3rd trimmers can't be follow-up for 6months because majority of them are close to their expected date of delivery).
2. All pregnant women who are already diagnosed with malaria will be excluded from the study.

Sample size determination
The sampling frame will be a list of all pregnant women attending antenatal clinic in UNTH, Enugu State, Nigeria. The sample size for continuous variables, such as knowledge and practice, the below formula for comparing two means by Lemeshow will be used (26). Sample size calculation is as follows;

$$n = \frac{(Z_{1-\alpha/2})\,(1-P) + Z1-\beta\,\sqrt{P_1\,(1-P_1) + P_2\,(1-P_2)}}{(P_1 - P_2)^2}$$

where:
$P = (P_1 + P_2) / 2 = (0.705+0.467) / 2 = 0.586$
P_1 = estimated utilization of ITNs in intervention group is = 0.705
P_2 = estimated utilization of ITNs in control group is = 0.467
$Z_{1-\alpha/2}$ = standard error when $\alpha = 0.05$ (95% Confidence Interval) = 1.96
$Z_{1-\beta}$ = standard error associated with power 80%= 1.282 ($\beta = 0.20$)
Therefore, the total sample size is 283.

Randomization and patient recruitment
Simple randomization will be used in this study, which will involve pregnant women attending antenatal clinic in UNTH, Enugu State, Nigeria (Figure 2). The research assistant will screen for eligibility, the inform pregnant women about the study and obtain informed consent from the pregnant women.

A method involving a random sequence generator program, overseen by a biostatistician working independently on a project within the Hospital Health

Information Unit, will manage the allocation sequence and allocation concealment. This process is designed to randomly assign the sample population to intervention and control groups in a 1:1 ratio. Allocation concealment will occur during randomization to minimize selection bias, ensuring that the researcher, clinician, and pregnant women remain unaware of their upcoming assignments. The task of concealment will be entrusted to an independent individual from the pharmacy department, who will employ a number code sequence within a sealed envelope. The study will exclusively include permanent residents of Enugu state to mitigate attrition and drop-out. The allocation sequence will be kept confidential from the research assistant enrolling participants, achieved through the use of sequentially numbered, opaque, sealed, and stapled envelopes. The pregnant women name and date of birth will be written on the envelope and recorded on a separate sheet of paper. The information containing the allocation codes will be made visible only after the corresponding envelopes are opened at the time of consultation, and this is only after the enrolled pregnant women complete all baseline assessments. The envelop will be kept in the pregnant women folder for subsequent follow-up.

Development of guidelines, SOP and training of research team

Development of guidelines and standard operating procedure (SOP) is cardinal to this study. Subsequent to the intervention, there will be development and validation of the training module for research assistants who will be employed for this study. Health education intervention in addition to routine clinic care will be used in this RCT as a means for improving ITNs use among pregnant women in the intervention group, while the control group will be left to receive their normal routine clinic care only.

A training module will be developed based on the Information on health care seeking behaviour, patients' illness responses (27) and validity in other to ensure that it is able to achieve the desired results for which it is intended; the module will be validated for content validity. The validation will be carried out by experts specifically experts from the field of epidemiology, infectious diseases and health promotion. Upon completion of the module validation, pre-testing of the module will be conducted among 2 nurses in the clinic who will not be part of the study. A total of four nurses involved in Antenatal Care Unit UNTH will be trained. They will be educated on the objective of the research and their view regarding the perceived benefits of delivering the intervention. The training procedure will encompass engaging in role-playing exercises and conducting discussions related to health education. Additionally, they will assess the questionnaire through a pre-test to ensure its validity.

Home based follow-up care intervention

The nurses using task-shifting strategy are the main human resource drivers for this study. Four nurses who have worked in the Antenatal Care Unit of UNTH for 1 year. They will be recruited based on merit and trained in counseling. Monday to Friday will be the working schedule with an average of 5 patients visit each day. Each enrolled participant will undergo follow-up visits at 3 and 6 months, totalling two rounds of follow-up. After randomization into the study's two arms and completion of the baseline assessment, the intervention group will receive home-based follow-up at 3 and 6 months (see Figure 2). While the intervention group will be advised to visit the hospital for follow-up every third month, some flexibility is allowed based on the managing physician's assessment. In contrast, the control group will not receive home-based follow-up care (see Figure 2), and their regular standard care at the hospital will persist. The overseeing doctor remains fully accountable for managing the clinic's appointment schedule and overseeing non-medication therapy. The control group will undergo a baseline assessment just like the intervention group. Nevertheless, after a period of 6 months, the control group will receive a home visit for the post-intervention assessment.

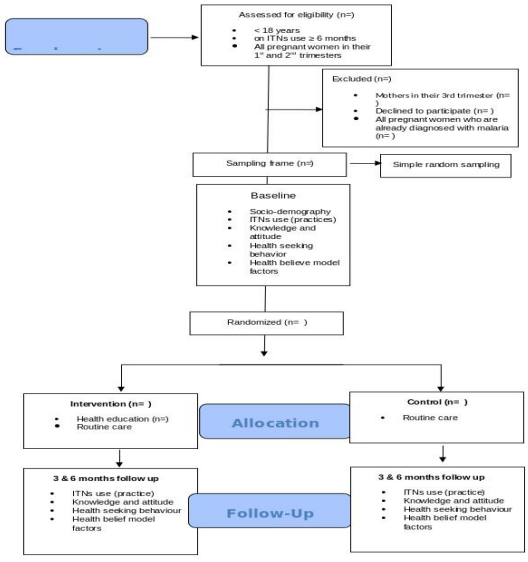

Figure 2: Study Flowchart showing randomization adapted from CONSORT (Schulz et al 2010).

Ethical Clearance

The Ethics Committee for Research Involving Human Subjects (JKEUPM) at Universiti Putra Malaysia granted approval for this study (UPM.TNCPI.800-2/1/7).

Data collection

An informed consent form will be given to the participants who willingly agree to participate in the study after which they will be asked to read and sign the form. Afterwards, the participants will be required

to fill up a structured pre-tested baseline questionnaire either in English or Igbo language and the research assistant will read out to those who cannot read but understands either of the language. The questionnaire will be organized into six segments, which include Socio-demographic information, the current awareness, attitudes, and practices regarding Malaria and Insecticide-Treated Nets (ITNs) among pregnant women, health-seeking behaviors, the framework of the health behavior model, and adherence to preventive measures for malaria involving the use of insecticide-treated nets. Amendments to the final questionnaire will be based on findings from the pretesting. The pregnant women will be required to fill up another follow-up questionnaire at 3rd and 6th months (follow-up). Information on patient's malaria status will be gotten from the pregnant women folder. The questionnaires will be distributed and collated by the research assistants. The assessment of internal consistency reliability through the use of the Cronbach's alpha index will involve evaluating reliability values, with a threshold of 0.70 or above considered valid. This criterion will serve as the standard for determining reliability (26).

The Pilot Study

A pilot study will first be conducted by administering the questionnaire on pregnant women who attend antenatal clinic in Royal hospital, Enugu State, Nigeria. A total of 30 pregnant women will be use for the plot study. This will be done to understand the questionnaire's wording and measurement, evaluate any ambiguity in the questions, carry out reliability. The pilot studies results will identify any modifications that are needed in the study instrument. The researcher will make the necessary modifications to the words that are not understood by the women.

Main outcome measurements

Treatment effects on the knowledge, attitude and practices towards the use of ITNs. Treatment effects on another intermediary outcome.

Data Analysis

The analysis of data will be conducted using SPSS version 23, with the application of the Intention to Treat (ITT) analysis concept for the final assessment. According to this approach, all patients in the intervention group will be analyzed based on their randomized treatment assignment, regardless of factors such as noncompliance, protocol deviations, attrition, or any other incidents post-randomization. The results will encompass descriptive analysis, featuring calculations of means, 95% confidence intervals (CI) of means, and frequencies of categorical variables.

Bivariate comparative analysis of the descriptive socio-demographic mean scores for both groups of patients will be performed using both independent student t-test and paired t-test at baseline, 3 months, and 6 months. Additionally, Repeated ANOVA will be employed to assess changes within the intervention group from baseline to 3 and 6 months post-intervention. Furthermore, it will be used to compare changes between the intervention group and the control group at 3 and 6 months post-intervention.

For a comprehensive evaluation of all independent variables and covariates, General Estimating Equation (GEE) will be utilized. GEE will be applied to assess changes over time and differences between groups, providing a thorough analysis of the study's outcomes.

DISCUSSION

The study aims to enhance knowledge, attitudes, and practices associated with the utilization of ITNs among pregnant women. This is critical for improving health outcomes as it can lead to increased uptake of ITNs, thereby reducing the risk of malaria and other infectious diseases. Health education plays a vital role in empowering individuals to make informed decisions about their health. By incorporating health education components into hospital-based care programs, researchers can promote positive health-seeking behaviors among pregnant women, ultimately leading to better health outcomes for both mothers and infants. The utilization of the Health Belief Model (HBM) in intervention studies is significant as it provides a theoretical framework for understanding health-related behaviors. By measuring various constructs of the HBM such as perceived susceptibility, severity, benefits, barriers, and cues to action, researchers can gain insights into the factors influencing pregnant women's decisions regarding the use of ITNs and other preventive measures.

The research by Watanabe et al. (29) revealed substantial variations in Susceptibility, Severity, Benefits, and Barriers between intervention and control groups in Vanuatu. Susceptibility refers to the likelihood of individuals contracting malaria, Severity indicates the seriousness of its impact, Benefits encompass advantages such as the use of insecticide-treated nets and malaria knowledge, while Barriers represent obstacles to preventive measures. These factors are critical in shaping behaviors towards malaria prevention, aiming to reduce anxiety and the disease burden, as highlighted by WHO (2022). Relating these constructs to the effects of health education interventions on insecticide-treated net utilization among antenatal pregnant women in a Nigerian teaching hospital, we can tailor our approach to address specific barriers, emphasize benefits effectively, and cater to varying levels of susceptibility and severity perceptions within the pregnant women.

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