American Journal of Applied Mathematics
2026, Vol. 14, No. 4, pp. 227–243
https://doi.org/10.11648/j.ajam.20261404.16

Research Article

Compartmental Modelling of Antenatal-care Interventions for Malaria in Pregnancy, Makurdi, Benue State, Nigeria

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Abstract

Malaria remains a serious public health concern contributing significantly to maternal and neonatal morbidity and mortality. Impact of malaria infection seems high in pregnant women due to their immunological changes that increases susceptibility to *plasmodium falciparum* infections and can be controlled with preventive interventions. This study evaluates antenatal-care (ANC) impact in mitigating malaria in pregnancy using SIRS-SI deterministic compartmental model that accounts for malaria interventions at different uptake of intermittent preventive treatment in pregnancy (IPTp). The equilibrium states and effective reproduction number were obtained using next-generation matrix while numerical simulations were done via RStudio in R using Makurdi data extracted from District Health Information Systems (DHIS-2) covering 2021 to 2023. The various interventions mitigated malaria in pregnancy with insecticide treated net (ITN) effective usage having the highest impact at early stage of IPTp uptake. Pregnant women were more proactive in taking IPTp first dose (IPTp-1) during ANC (average of 67.7%) than subsequent doses (50.8% and 30.9% respectively). Artemisinin-based combination therapy (ACT) aids recovery of those infected while IPTp significantly reduced susceptibility of pregnant women. Infected cases were reduced from 43.1% to 38.3%, 38.7% and 31.5% in proportion to the susceptible that took IPTp-1, IPTp-2 and IPTp-3 respectively. Mixed intervention generated better outcome for malaria control in pregnancy relative to the impact of each intervention done singly. Consequently, early preventive interventions during ANC, especially ITN effective usage and IPTp uptake should be strongly encouraged to minimize malaria infection risk and ACT support given to those infected whenever necessary.

Keywords

Malaria in Pregnancy, Infectious Disease, Intervention, Antenatal-care, Mathematical Model

1. Introduction

Malaria infection is an infectious disease transmitted by *Plasmodium* parasites to humans through the bites of infected female *Anopheles* mosquitoes. It is a protozoan vector-borne disease that is preventable and curable though it is responsible for several death cases in Africa and other parts of the world [1, 2]. Malaria infection is known to be a growing global concern because of its ability to emerge and lead to serious consequences in the lives of its host. According to research, about 12.7 million pregnancies across the globe suffered from malaria infection as at 2022 with the African region bearing most

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Received: 24 June 2026; **Accepted:** 7 July 2026; **Published:** 24 July 2026

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of the burden which account for the large number of cases and death recorded within the region [3].

Malaria is enlisted as the most common and potentially most serious infection occurring in pregnancy in many sub-Saharan African countries [2, 4]. Nigeria accounts for about 27% of malaria infection and 31% of malaria-related deaths globally [5, 6]. Malaria is caused by *Plasmodium* species, predominantly *Plasmodium falciparum*. In Nigeria it is transmitted mainly by the mosquito vectors of the *Anopheles gambiae* complex and the *Anopheles funestus* group. The complexity of malaria infection transmission pattern in Nigeria varies according to the diversity of the ecological system which account for the heterogeneity of the transmission of malaria across the various States of Nigeria and the required intervention strategies relevant to each context [7].

Benue State is situated in the North-Central region of Nigeria with Makurdi as the Capital. The State operates an agrarian economy with about 80% of her population engaging in agricultural activities as farmers. The tropical climate conditions indicate an annual rainfall of 1,314.3 millimeters approximately with an average temperature between 23 - 37 ℃ [8-10]. Malaria infection in Makurdi peaks during the rainy season, between April and October and is influence by the region tropical climate, the confluence of the River Benue, agricultural practices and rapid urbanization thus creating favourable ecological conditions that enhances mosquito breeding sites and habitats [8, 11]. The World Health Organization reports malaria prevalence of 34% (RDT records) and 17% (microscopy records) in Benue State with an incidence rate of 257.2 per 1000 population.

Alom *et al*. [8] and Adaji *et al*. [12] classified Makurdi Local Government Area (LGA) as region with high to moderate malaria transmission intensity with substantial heterogeneity between the urban and the peri-urban areas. Some studies revealed that the most dominant species within the region is the *Plasmodium falciparum*, the leading cause of complications during pregnancy [1, 3, 8]. Complications from *Plasmodium falciparum* infection in pregnancy include maternal anaemia, miscarriages, premature delivery and infant low birth weight with high risk of maternal and infant mortality [1, 3, 13, 14]. Therefore, malaria infection during pregnancy poses substantial risks not only to the mother, but also to her developing fetus and the newborn [3, 4].

Pregnant women experience higher risk compared to other adults and are more vulnerable to malaria simply because of the immunological changes they experience and the presence of the placenta which provides favourable environment for *Plasmodium falciparum* and *Plasmodium vivax* [3, 15-17]. In low transmission settings or cases with no immunity, the *Plasmodium falciparum* malaria can progress rapidly from uncomplicated to severe malaria infection with risk 2-3 times higher than a non-pregnant woman [18, 19]. The importance of antenatal-care (ANC) services cannot be overlooked. The most effective control strategic of malaria in pregnancy is the comprehensive intervention package recommended by World Health Organization which integrate interventions into the strong platform of ANC services [2, 20].

The malaria intervention strategies mostly employed in Nigeria include: the usage of insecticide treated nets (ITNs) distributed across the States through mass distribution techniques, indoor residual spraying (IRS), and the artemisinin-based combination therapy (ACT). The current preventive strategies recommended by World Health Organization (WHO) include intermittent preventive treatment in pregnancy (IPTp) with sulfadoxine-pyrimethamine (SP) and use of insecticide-treated nets (ITNs). Despite all the numerous efforts put in place to curtail the high infection rate of malaria transmission, it has persisted overtime at endemic level in major areas of the country [6, 12, 21]. Research by scholars and WHO report indicated that malaria prevalence among pregnant women has persisted in Makurdi with inconsistent attendance at ANC and many pregnant women do not complete the recommended 3+ IPTp doses. Consequently, the uptake of malaria interventions such as IPTp and ITNs during ANC remain suboptimal [22-24].

Health education intervention promotes IPTp adherence and uptake of the recommended complete dose during pregnancy. Furthermore, the health personnel (nurses, midwives, doctors and community health workers) play crucial role in controlling malaria infections in pregnancy during ANC. They provide counselling in ITN effective usage, administer IPTp at the required time interval, test for malaria infection, prescribe and disperse antimalarials along with managing of complicated malaria cases. In addition, they provide adequate service documentation during each ANC visit as reference for future consultations and guide [25, 26]. Major challenge of the system is the supply chain management, that is inadequate stock of SP, ITNs, diagnostic tests and treatment drugs and lack of adequate human resources leading to longer waiting time and discouraged attendance at the subsequent ANC visits [19]. Studies have shown alarmingly high prevalence rates among pregnant women, reporting 68.3% infection rate among antenatal clinic attendees [22, 27].

Despite high malaria burden and suboptimal ANC uptake in Makurdi, there seems to be no existing publications on mathematical compartmental models that studied malaria infection in pregnancy with localized Makurdi data at the various stages of IPTp dosage as recommended by WHO. Most of the available modelling research works on malaria in Nigeria aggregate at the State and National level with only few considering Makurdi LGA. Aside the limited number of existing literatures on mathematical models designed with Makurdi-specific calibrated data, to our knowledge there is no prior study that evaluated the influence of ANC interventions among pregnant women in Makurdi using SIRS-SI compartmental model framework that incorporated the three stages of IPTp dose (the WHO recommended minimum) with calibrated District Health Information Systems (DHIS-2) malaria incidence data of pregnant women in Makurdi. This study, therefore, filled this gap by evaluating Compartmental Modelling of Antenatal-care Interventions for Malaria in Pregnancy with a case Study of Makurdi, Benue State, Nigeria.

Mathematical modelling has contributed enormously to research on malaria infection and has become an essential tool in understanding malaria transmission dynamics and evaluating intervention strategies [22, 28-30]. Mathematical modelling is a process in which problems in real world scenario are translated into some precise mathematical concepts or form known as model. Models are tools necessary for integrating and translating scientific data into policy-relevant outcomes. They are represented by algebraic equations, differential equations, statistical distributions, or computational algorithms [31-34]. Mathematical modelling provides a quantitative framework in malaria epidemiology for the transmission simulation and the evaluation of potential impact of various malaria control intervention strategies. The Ross basic mathematical model (SIR) formed the foundation for malaria modelling in pregnancy which provides the hierarchical structure of deterministic mathematical model with varying complexity levels and employs ordinary differential equations as representation of the epidemiological compartments describing the malaria incidence patterns and transmission dynamics [35]. Various modelling approaches have been used to assess different intervention impacts, optimize resource allocation, and inform target product profiles for new malaria interventions [36-40].

Compartmental models are the most common types comprising of different compartments divided based on the infection status of both the human and mosquito population. The flow from one compartment to the other is described by the differential equation [8, 41-47]. This research paper aim at developing a mathematical compartmental model with the SIRS-SI framework to assess the influence of ANC interventions, ITN usage, IPTp uptake at different doses and ACT aiding recovery of infected pregnant women during ANC, in mitigating malaria infection among pregnant women in Makurdi.

2. Material and Methods

This study employed a retrospective secondary data analysis combined with deterministic mathematical modelling to evaluate the impact of antenatal-care-based malaria interventions. The model used the bi-directional transmission mechanism: human-to-mosquito and mosquito-to-human transmission. The transmission rates were modelled using the mass action terms with appropriate contact rates.

2.1. Study Area

Benue State has 23 Local Government Areas (LGAs) with Makurdi being the capital territory. The selection of Makurdi LGA as the study area was done using severity of cases as an anchor criterion.

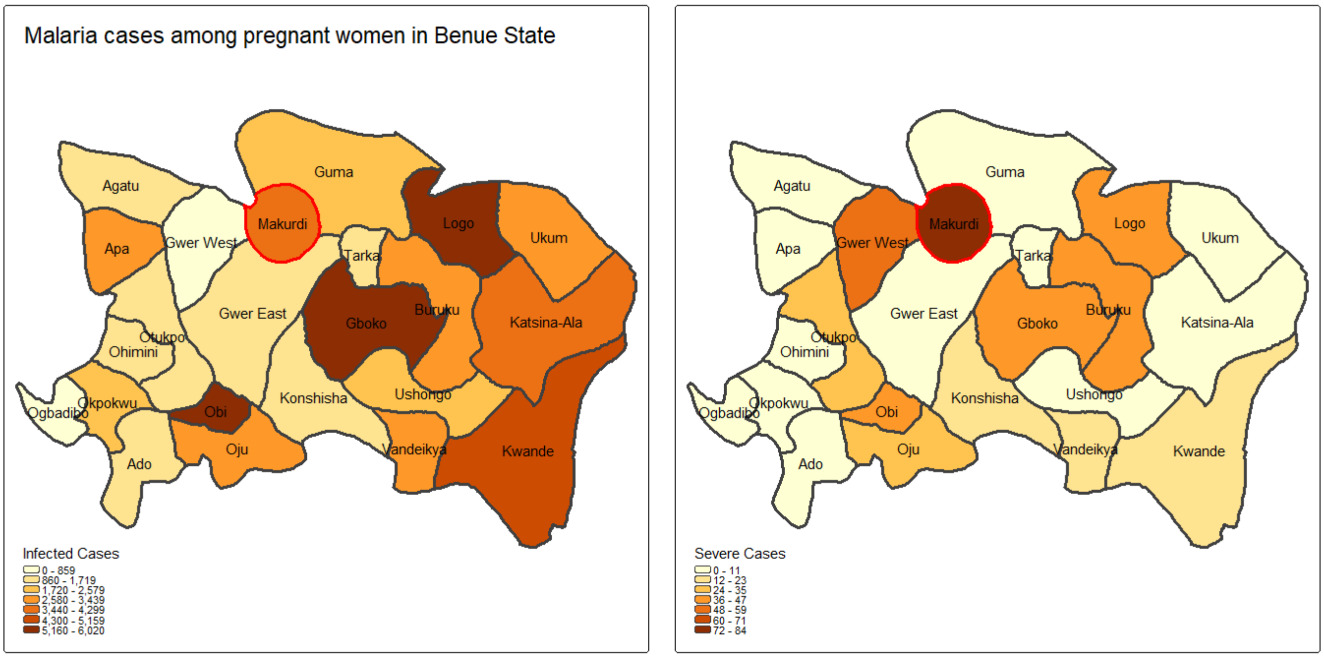

***Figure 1**. The Map of Benue State showing the total number of incidence and severe cases of malaria in pregnant women respectively within the 23 Local Government Areas.*

Makurdi recorded the highest total number of reported severe cases of malaria in pregnant women within the study period (2021 to 2023) though it had less total number of incidence cases in comparison to Logo, Gboko and Obi Local

Government Areas as captured by the geospatial maps in Figure 1 obtained using the malaria data for Benue State extracted from DHIS-2.

2.2. Population Size Estimate

Since the malaria monthly data for confirmed uncomplicated and severe cases of pregnant women in Makurdi used in the research work as extracted from DHIS-2 platform covers reported cases from 2021 to 2023, the population figure considered for the analysis was extracted from the 2021 population record of Makurdi. As captured in the Nigeria 2006 census by the National Bureau of Statistics [48], the total population of Benue State and Makurdi LGA were 4,219,244 and 297,398 in 2006 respectively. The Nigeria population projections and demographic indicators [49] projected the total population for Benue State in 2021 as 6,023,643 which by proportion gives a projection of 424,582 as the total population of Makurdi LGA in 2021.

2.3. Data Sources and Variables

The data extracted from DHIS-2 covers the malaria monthly data for confirmed uncomplicated and severe cases of pregnant women, the antenatal-care records for uptake of IPTp doses (IPTp-1, IPTp-2, IPTp-3) and the number of pregnant women clinically diagnosed with malaria treated with ACT during ANC visit within the period of three years, 2021 to 2023 and was processed on Microsoft Excel sheets to conform with R programming format for analysis. The model parameters were obtained from secondary sources while the values for the unavailable parameters were estimated by fitting the model equation using regression method via the application of RStudio in R programming software. The data obtained were also used for the analysis, evaluating the impact of the various malaria preventive interventions and ACT treatment, and compared outcomes across scenarios.

2.4. Model Structure

The study developed SIRS-SI deterministic compartmental model using ordinary differential equations to represent malaria transmission dynamics among pregnant women. An advanced epidemiological framework extended from the basic SIR model. The model includes compartments for susceptible, infected, and removed (recovered and those that transited as a result of IPTp uptake providing prophylactic protection) pregnant women, with the vector incorporated through structured compartments of susceptible and infected mosquito as captured by Figure 2.

The compartment S denotes the susceptible, I the infected and R the removed population respectively. The subscripts, “0” represents the category of women with no uptake of IPTp at the various compartments, that is, pregnant women not protected via IPTp doses. While the subscripts “1”, “2”, “3” connote scenarios representing pregnant women with prophylactic protection through the uptake of first, second and third dose of IPTp respectively. Lastly, the subscript “v” denotes the segment representing the vector population. The total human population is denoted by N.

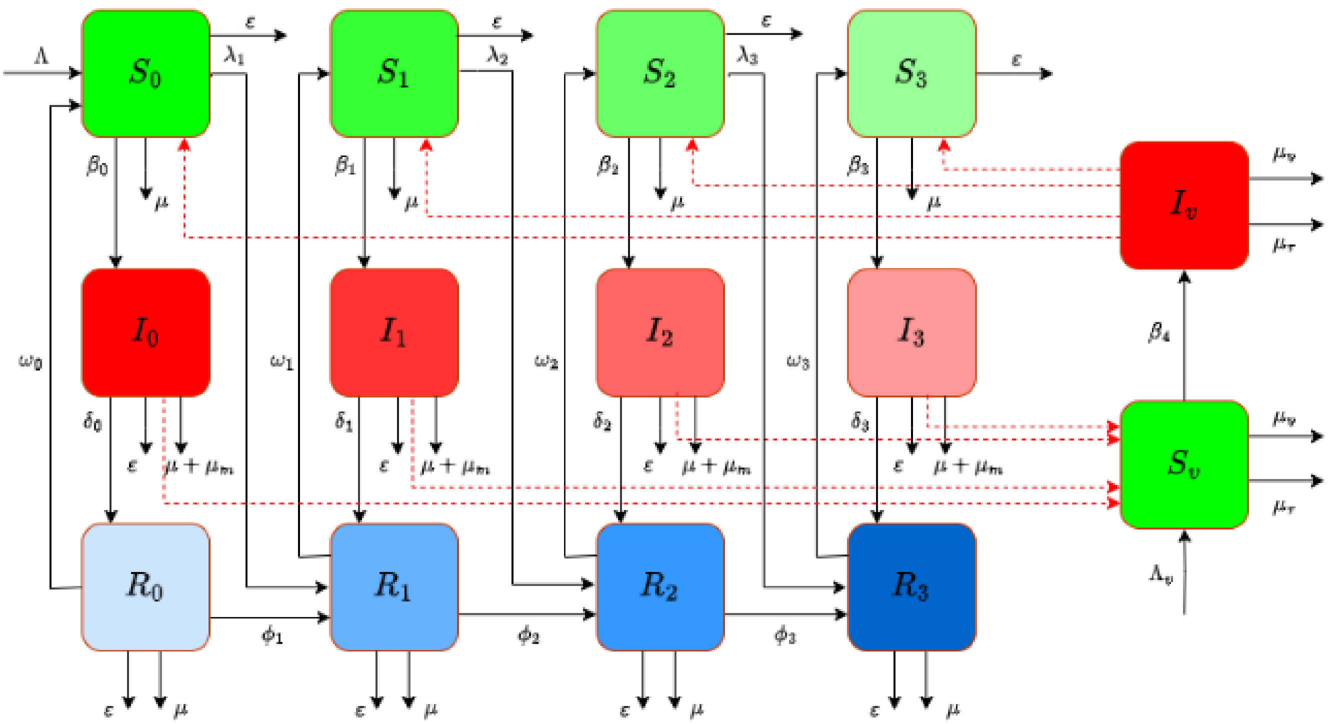

Figure 2. *The schematic flow diagram of the model.*

The model parameters include the recruitment rates (Λ, Λ_v), malaria transmission rates (β_i, i = 0, 1, 2, 3, 4), removal rates due to natural death, malaria infection and effectiveness of ITN in killing mosquito (μ, μ_m, μ_τ), the rate of ITN effective usage (τ), the effective rates of IPTp intervention (a_i, i = 1, 2, 3), rates of IPTp uptake among susceptible pregnant women (λ_i, i = 1, 2, 3), recovery rates aided by ACT treatment (δ_i, i = 0, 1, 2, 3), the immunity waning rates of pregnant women (ω_i, i = 0, 1, 2, 3), the rates at which those recovering received educational insight that encouraged their participation in the subsequent doses of IPTp uptake (ϕ_i, i = 1, 2, 3), and the removal rate as a result of healthy baby delivery (ε).

The model assumes that the total pregnant human population is susceptible to malaria infection, the recovered population loses their immunity after a period and becomes susceptible again to the infection, the population of pregnant women who took part in the uptake of IPTp obtained some level of protection against malaria infection for some certain period of time hence, transit to the removed compartment until they become vulnerable again. The study considered 42 days as the lifespan of mosquitoes which gave a death rate of 0.7143 per month, the mosquito to human population ratio is assumed as 3 per person. The infectivity rate of the mosquito population is put at 4.8% as extracted from Manyi *et al*. [50] and the recovery of infected human is assumed to be 3 days while the rate of human death due to malaria infection as 1.2 per 1000 population.

The model equation is derived using the flow diagram in Figure 2 and after simplification obtained the system of equations as defined in equation (1),

$$\begin{aligned}
\frac{dS_0}{dt} &= \Lambda + \omega_0 R_0 - \frac{\beta_0 S_0 I_v}{N} - x_0 S_0,\\
\frac{dI_0}{dt} &= \frac{\beta_0 S_0 I_v}{N} - y_0 I_0,\\
\frac{dR_0}{dt} &= \delta_0 I_0 - z_0 R_0,\\
\frac{dS_1}{dt} &= \omega_1 R_1 - \frac{\beta_1 S_1 I_v}{N} - x_1 S_1,\\
\frac{dI_1}{dt} &= \frac{\beta_1 S_1 I_v}{N} - y_1 I_1,\\
\frac{dR_1}{dt} &= \lambda_1 S_0 + \phi_1 R_0 + \delta_1 I_1 - z_1 R_1,\\
\frac{dS_2}{dt} &= \omega_2 R_2 - \frac{\beta_2 S_2 I_v}{N} - x_2 S_2,\\
\frac{dI_2}{dt} &= \frac{\beta_2 S_2 I_v}{N} - y_2 I_2,\\
\frac{dR_2}{dt} &= \lambda_2 S_1 + \phi_2 R_1 + \delta_2 I_2 - z_2 R_2,\\
\frac{dS_3}{dt} &= \omega_3 R_3 - \frac{\beta_3 S_3 I_v}{N} - x_3 S_2,\\
\frac{dI_3}{dt} &= \frac{\beta_3 S_3 I_v}{N} - y_3 I_3,\\
\frac{dR_3}{dt} &= \lambda_3 S_2 + \phi_3 R_2 + \delta_3 I_3 - z_3 R_3,\\
\frac{dS_v}{dt} &= \Lambda_v - \frac{\beta_4 S_v (I_0 + I_1 + I_2 + I_3)}{N} - y_4 S_v,\\
\frac{dI_v}{dt} &= \frac{\beta_4 S_v (I_0 + I_1 + I_2 + I_3)}{N} - y_4 I_v
\end{aligned} \tag{1}$$

where $\beta_0 = \beta(1-\tau)$, $\beta_1 = \beta(1-\tau)(1-a_1)$, $\beta_2 = \beta(1-\tau)(1-a_2)$, $\beta_3 = \beta(1-\tau)(1-a_3)$, $\beta_4 = \beta_v(1-\tau)$, $x_0 = \varepsilon + \mu + \lambda_1$, $x_1 = \varepsilon + \mu + \lambda_2$, $x_2 = \varepsilon + \mu + \lambda_3$, $x_3 = \varepsilon + \mu$, $y_0 = \delta_0 + \varepsilon + \mu + \mu_m$, $y_1 = \delta_1 + \varepsilon + \mu + \mu_m$, $y_2 = \delta_2 + \varepsilon + \mu + \mu_m$, $y_3 = \delta_3 + \varepsilon + \mu + \mu_m$, $y_4 = \mu_v + \mu_\tau$, $z_0 = \omega_0 + \varepsilon + \mu + \phi_1$, $z_1 = \omega_1 + \varepsilon + \mu + \phi_2$, $z_2 = \omega_2 + \varepsilon + \mu + \phi_3$, $z_3 = \omega_3 + \varepsilon + \mu$,

satisfying the initial conditions defined in equation (2).

$$\begin{array}{lll}
S_0(0) > 0, & I_0(0) \geq 0, & R_0(0) \geq 0,\\
S_1(0) \geq 0, & I_1(0) \geq 0, & R_1(0) \geq 0,\\
S_2(0) \geq 0, & I_2(0) \geq 0, & R_2(0) \geq 0,\\
S_3(0) \geq 0, & I_3(0) \geq 0, & R_3(0) \geq 0,\\
S_v(0) > 0, & I_v(0) \geq 0 &
\end{array} \tag{2}$$

2.5. Model Analysis and Equilibrium States

Evaluating the model equation at the equilibrium state gave two steady states: the disease-free steady state.

$$k_0 = \left(S_{0_0}^{*}, I_{0_0}^{*}, R_{0_0}^{*}, S_{1_0}^{*}, I_{1_0}^{*}, R_{1_0}^{*}, S_{2_0}^{*}, I_{2_0}^{*}, R_{2_0}^{*}, S_{3_0}^{*},, I_{3_0}^{*}, R_{3_0}^{*}, S_{v_0}^{*}, I_{v_0}^{*}\right)$$

and the endemic steady state

$$k_* = \left(S_0^*, I_0^*, R_0^*, S_1^*, I_1^*, R_1^*, S_2^*, I_2^*, R_2^*, S_3^*,, I_3^*, R_3^*, S_v^*, I_v^*\right)$$

The details of the disease-free steady state obtained are as follows:

$$S_{0_0}^{*} = \frac{\Lambda}{x_0}, \; S_{1_0}^{*} = \frac{\Lambda\lambda_1\omega_1}{x_0 x_1 z_1}, \; S_{2_0}^{*} = \frac{\Lambda\lambda_1\omega_2(\lambda_2\omega_1 + \phi_2 x_1)}{x_0 x_1 x_2 z_1 z_2}, \; S_{3_0}^{*} = \frac{\Lambda\lambda_1\omega_3(\lambda_2\omega_1 + \phi_2 x_1)(\lambda_3\omega_2 + \phi_3 x_2)}{x_0 x_1 x_2 x_3 z_1 z_2 z_3}, \; S_{v_0}^{*} = \frac{\Lambda_v}{y_4}, \; I_{0_0}^{*} = 0, \; I_{1_0}^{*} = 0, \; I_{2_0}^{*} = 0, \; I_{3_0}^{*} = 0, \; I_{v_0}^{*} = 0, \; R_{0_0}^{*} = 0, \; R_{1_0}^{*} = \frac{\Lambda\lambda_1}{x_0 z_1}, \; R_{2_0}^{*} = \frac{\Lambda\lambda_1(\lambda_2\omega_1 + \phi_2 x_1)}{x_0 x_1 z_1 z_2}, \; R_{3_0}^{*} = \frac{\Lambda\lambda_1(\lambda_2\omega_1 + \phi_2 x_1)(\lambda_3\omega_2 + \phi_3 x_2)}{x_0 x_1 x_2 z_1 z_2 z_3} \tag{3}$$

Furthermore, knowing that malaria transmission follows the seasonal pattern, the seasonality of the malaria data was accounted for in the model analysis by considering a seasonality factor defined by the conventional wave equation use in determining the amplitude of oscillation,

$$\beta_i(t) = \beta_i[1 + \Omega\cos(\eta t + \theta)], \; i = 0,1,.,4$$

where Ω represents the amplitude, η denote the frequency and θ represents the phase shift in the oscillation. This is similar to the process recorded in Ochieng [51]. The effective reproduction number, R_e is obtained using the next-generation matrix. The method determines the value of R_e as the spectral radius, ρ of the next-generation matrix [47] as

$$R_e = \rho(FV^{-1}) \tag{4}$$

Consequently, applying the next-generation matrix, the effective reproduction number for the model equation (2) was obtained using the mathematical expression defined in equation (4) representing the dominant eigenvalue of the matrix (FV^{-1}) where the matrix F and V were generated from equation (2) using "Google Colab" to ease the computation processes and evaluated at the disease-free equilibrium steady state given in equation (3) to obtain the effective reproduction number, R_e as

$$R_e = \sqrt{\frac{\Lambda_v \beta_4 m_0 (y_2 y_3 m_1 + y_0 y_1 m_2)}{\Lambda y_0 y_1 y_2 y_3 (y_4 m_3)^2}} \tag{5}$$

where $m_0 = x_0 x_1 x_2 x_3 z_1 z_2 z_3$, $m_1 = x_2 x_3 z_2 z_3 (\beta_0 x_1 y_1 z_1 + \beta_1 y_0 \lambda_1 \omega_1)$, $m_2 = \lambda_1(\lambda_2 \omega_1 + \phi_2 x_1)[\beta_2 \omega_2 x_3 y_3 z_3 + \beta_3 \omega_3 y_2 (\lambda_3 \omega_2 + \phi_3 x_3)]$, $m_3 = x_2 x_3 z_2 z_3 (\lambda_1 x_1 + x_1 z_1 + \lambda_1 \omega_1) + \lambda_1(\lambda_2 \omega_1 + \phi_2 x_1)\ [x_3 z_3 (x_2 + \omega_2) + (\lambda_3 \omega_2 + \phi_3 x_2)(x_3 + \omega_3)]$.

Furthermore, the sensitivity analysis of the model equation parameters was done to determine the most influential malaria intervention parameter on the system dynamics using R_e through the sensitivity analysis expression.

$$S_x = \frac{\partial R_e}{\partial x} \times \frac{x}{R_e} \tag{6}$$

The RStudio with R version 4.4.0 was further used for the model numerical simulation. The model was simulated deterministically using the "vode" method via the "deSolve" library in the R programming platform.

3. Results

3.1. Descriptive Epidemiology of Malaria Data

The model is calibrated using historical malaria data extracted from DHIS-2 covering pregnant women in Benue State, Nigeria within the targeted period of this study, from 2021 to 2023. Geospatial mapping and bar charts were employed via the application of R programming code to explore the prevalence of malaria infection among pregnant women during antenatal-care (ANC) visit and the uptake of IPTp, ITNs usage and the administration of ACT.

The data for malaria cases and the various interventions (ACT administration and the uptake of IPTp at different dose during ANC visit) in the various LGAs of Benue State as extracted from DHIS-2 gives the results in Figure 3 using geospatial map for a pictorial view of the results.

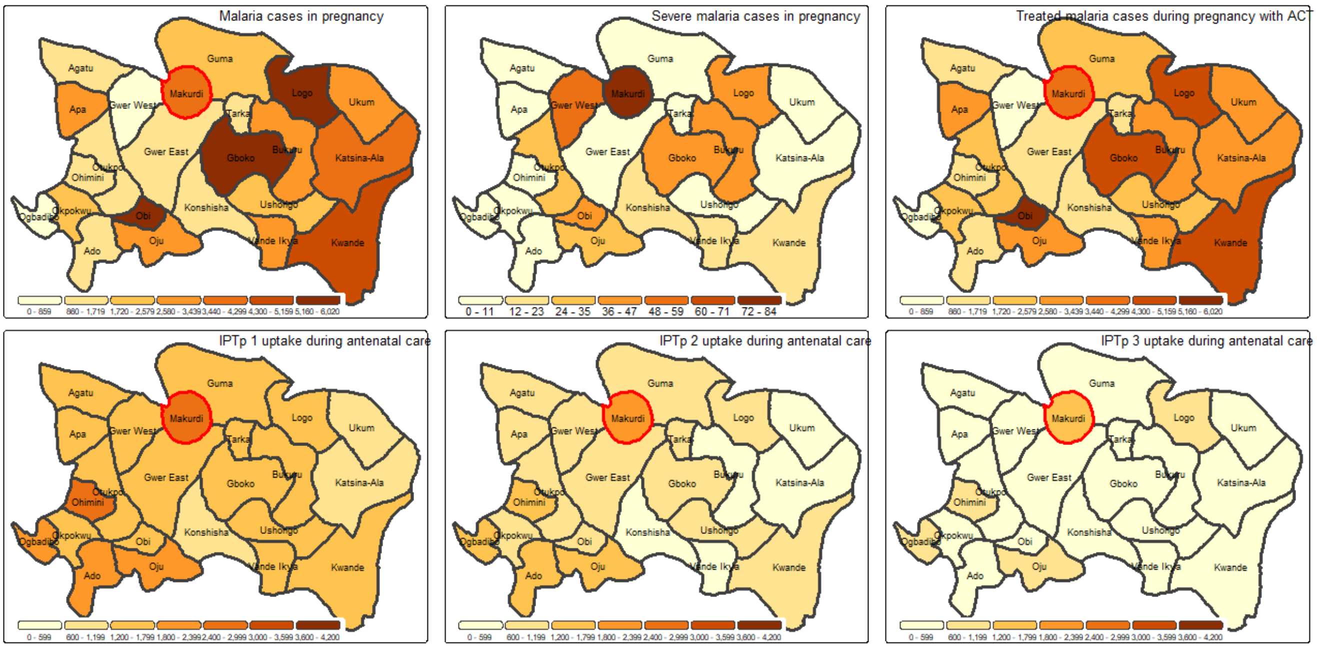

Figure 3. *The Map of Benue State showing the total of malaria cases, ACT intervention and IPTp uptake in the 23 Local Government Areas.*

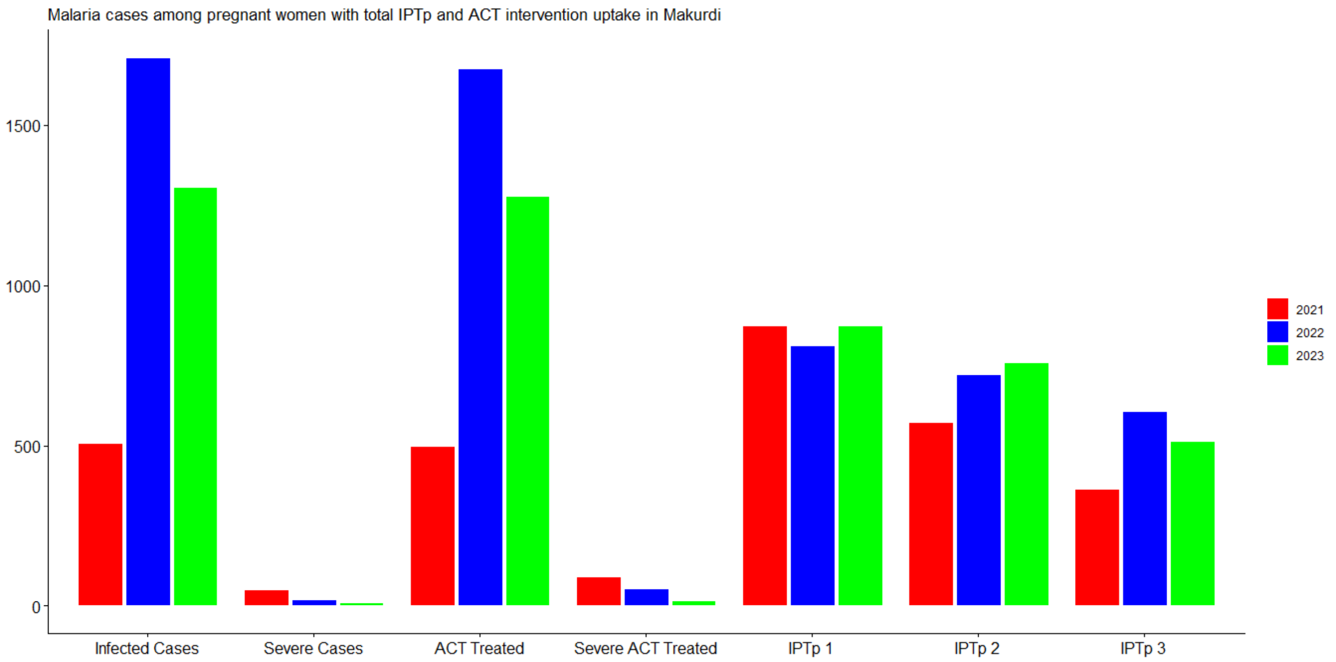

Figure 4*. The total yearly reported malaria cases in Makurdi and the various interventions.*

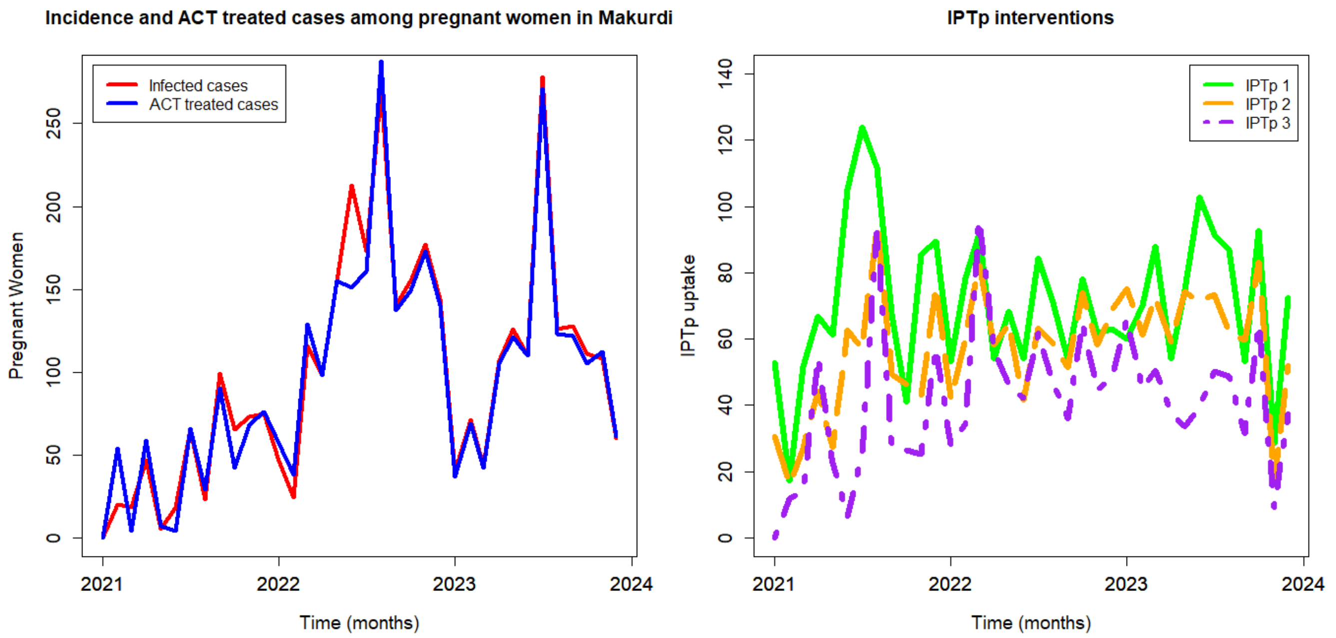

Figure 5*. The monthly total recorded malaria incidence cases in Makurdi and the interventions.*

Consequent upon the severity of malaria cases recorded across the various LGAs, Makurdi recorded the highest total number of severe cases from 2021 to 2023 even though the total number of incidence cases recorded within this period is less in comparison with other high-burden LGAs such as Gboko, Logo, Obi, among other LGAs. Hence, the choice of Makurdi LGA over Obi, Logo and Gboko which recorded higher number of total malaria incidence cases within the study period.

The distribution of the total yearly reported malaria cases in the selected LGA, and the various interventions are captured in Figure 4 using bar chart. Whereas the monthly data for the incidence cases and the interventions administered in curtailing the spread and impact of malaria infection is shown by the plot in Figure 5.

3.2. Model Calibration and Validation Results

The time series decomposition simulation of the incidence data into trend, random and seasonal components was done to ascertain the seasonality of the data set. The result obtained shows that the data is seasonal as shown in Figure 6. This was done to justify the usage of seasonality factor in the model equation.

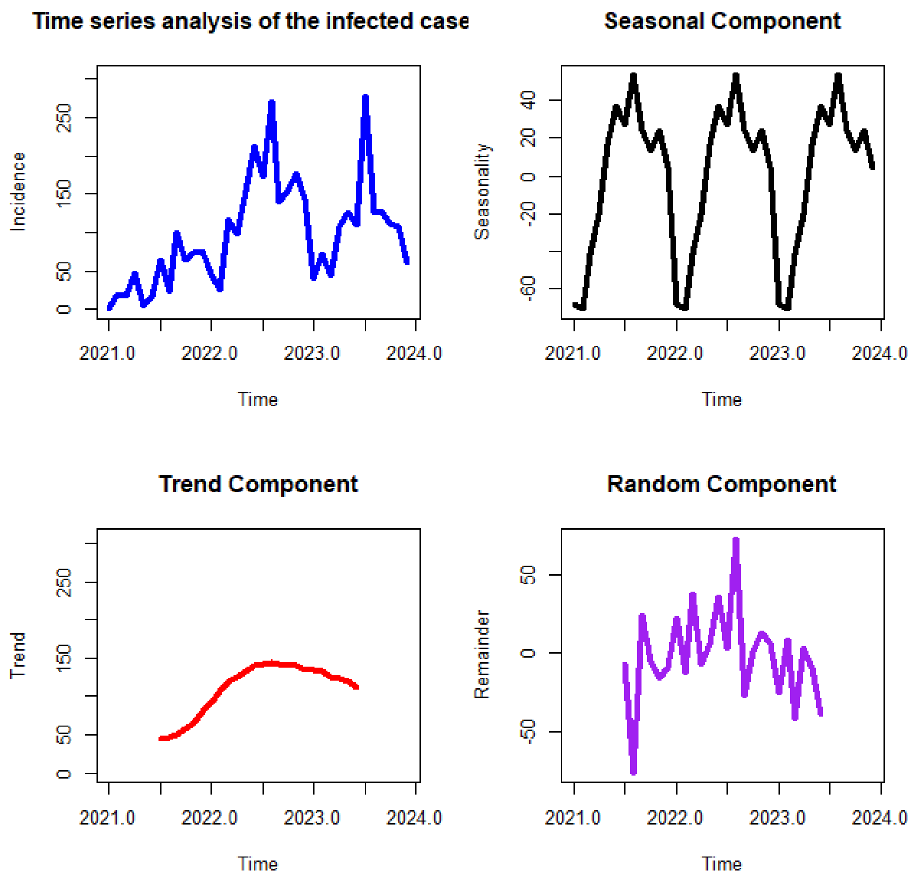

Figure 6. *Time series decomposition of the incidence cases into trend, random and seasonal components.*

The model simulation for the selected LGA was fitted using the Non-linear Least Squares Method (nlsLM) via a code generated in RStudio. The outcome of the analysis is captured in Figure 7 and the values of the initial state variables given in Table 1 along with the fitted parameter values extracted from the outcome of the curve fitting. In addition to the initial assumptions of the model, the administration of ACT is considered to be uniform across the different compartments of concern, before and after each dose of IPTp uptake. The total number of infected cases extracted from the data and the fitted curve are given in Table 2 showing slight difference in the values with a correlation of 74.5%. The model validation was done by comparing model predictions with observed cases.

As earlier mentioned, the study period covers 2021 to 2023 and the total population of Makurdi in 2021 was projected at 424,582. Using the information for the female population in the age group of 15 to 49 and the fertility rate extracted from the Nigeria population projections and demographic indicators [49] gives the total population of pregnant women, N in 2021 as 50.2% x 4.08% x 424,583 = 8,696 with a monthly recruitment rate of 725 pregnant women.

Table 1. *The initial values of state variables for the selected LGA and the model parameters.*

Initial States		**Known Parameters**		**Fitted Parameters**	
Variables	**Values**	**Symbols**	**Values**	**Symbols**	**Values**
$N(0)$	8,696	Λ	725	β	0.615818
$S_0(0)$	4,780	Λ_v	2,175	β_v	11.011331
$I_0(0)$	12	μ	0.0009	μ_τ	0.003081

Initial States		Known Parameters		Fitted Parameters	
Variables	Values	Symbols	Values	Symbols	Values
$R_0(0)$	0	μ_m	0.0012	δ	0.109259
$S_1(0)$	1,484	μ_v	0.7142	ω_0	0.5107
$I_1(0)$	3	τ	0.57	ω_1	0.2123
$R_1(0)$	0	ε	0.00267	ω_2	0.0367
$S_2(0)$	1,388	λ_1	0.171	ω_3	0.0125
$I_2(0)$	3	λ_2	0.16	ϕ_1	0.171
$R_2(0)$	0	λ_3	0.118	ϕ_2	0.16
$S_3(0)$	1,024	a_1	0.00736	ϕ_3	0.118
$I_3(0)$	2	a_2	0.6158	Ω	1.069223
$R_3(0)$	0	a_3	0.07357	ω	0.402168
$S_v(0)$	26,028			θ	1.106852
$I_v(0)$	60				

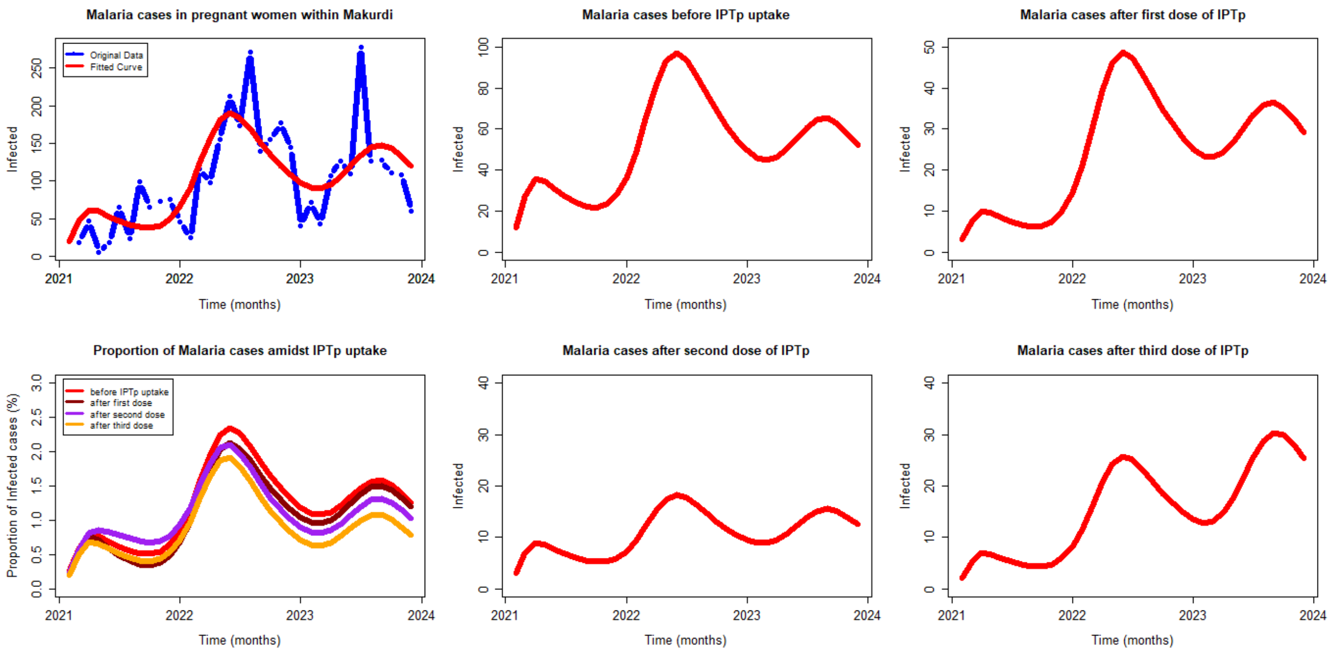

Figure 7. Dynamics for infected pregnant women in Makurdi LGA (DHIS-2) and the fitted curve obtained via numerical simulation.

Table 2. A comparison of the total number of infected cases (2021 - 2023) extracted from DHIS-2 and model simulation.

Source	Total Number of Infected Cases
DHIS-2 value	3,528
Simulated value	3,589

3.3. Reproduction Number and Sensitivity Analysis

The application of the parameter values given in Table 1 and those extracted from the fitted curve gave the effective reproduction number of 0.403 which is less than one, that is, $R_e < 1$ for the disease-free steady state. Indicating that with malaria interventions the disease will gradually die out of the population. Whereas, using the incidence cases and the library

(R0) in R programming software to determine the basic reproduction number of the incidence cases gave $R_b = 1.282654$ with the confidence interval of $[1.272589, 1.292943]$, indicating that $R_b > 1$ hence confirming an endemic state in Makurdi, Benue State, Nigeria which could be controlled with effective interventions.

The sensitivity analysis was done via "Google Colab" using the expression in equation (6) and the parameter values as defined in Table 1. The result obtained is shown in Figure 8 via a bar chat demonstrating the various sensitivity level of the parameters.

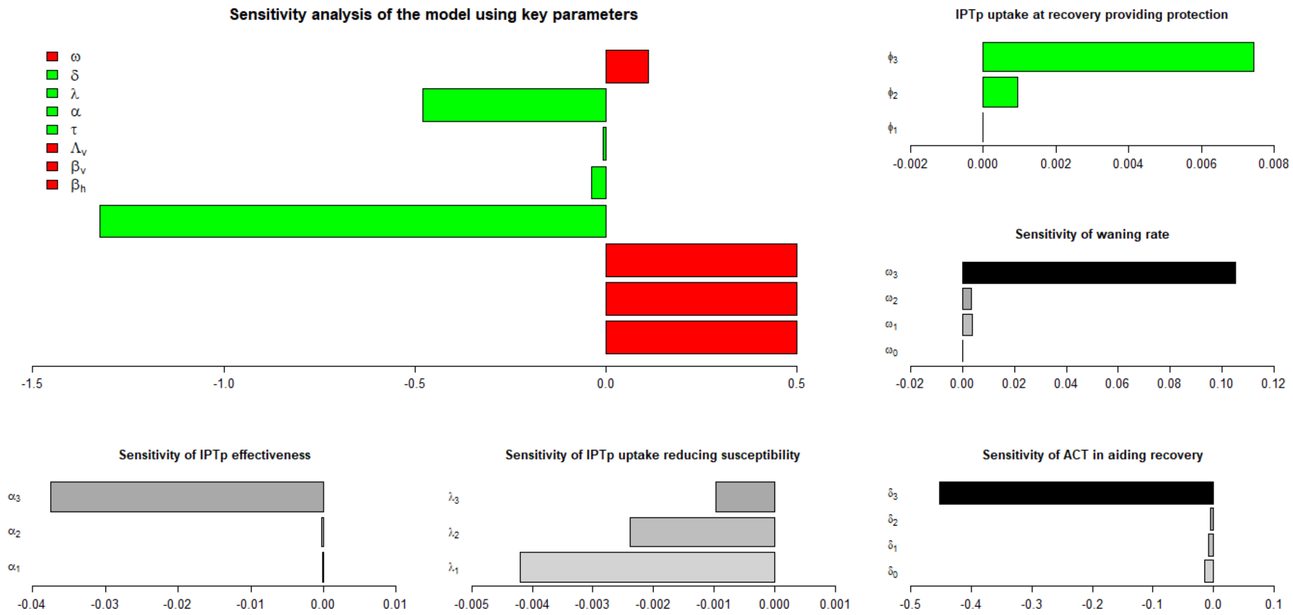

Figure 8. *The sensitivity of the model parameters on* R_e.

3.4. Scenario Analysis and Optimization

The intervention parameters in the model equation were analyzed to show their various impacts on the disease dynamics using the parameter values obtained from the fitted curves, details are captured in Figures 9 and 10 (also see Table 3).

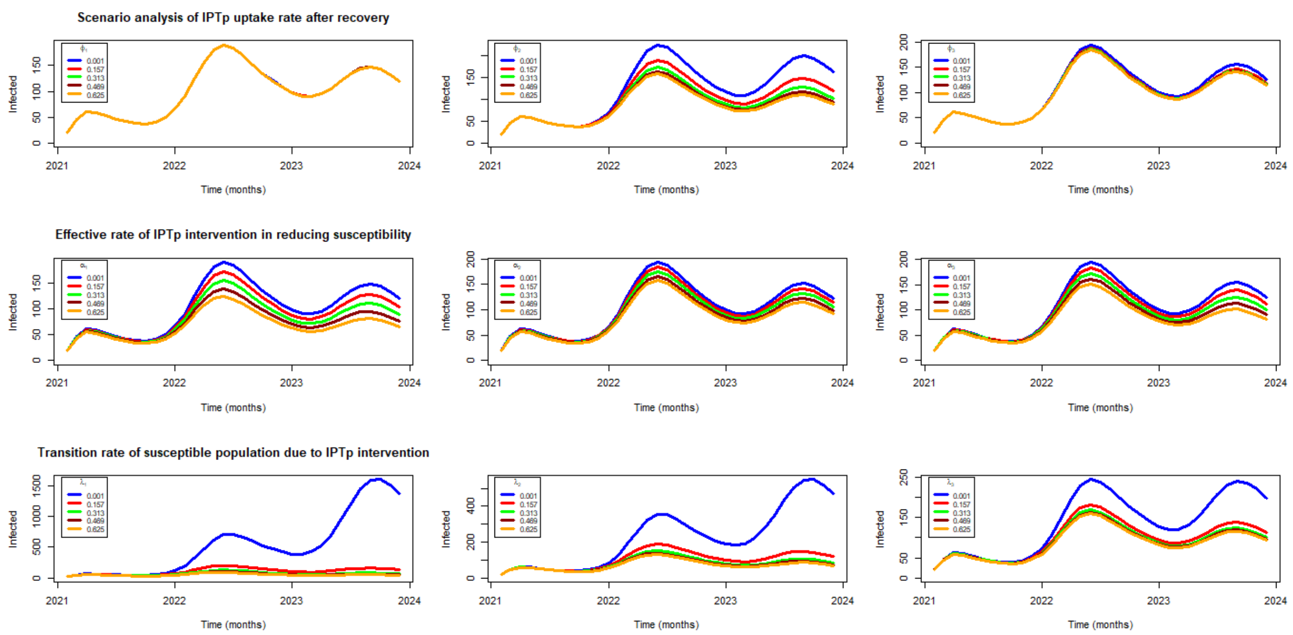

Figure 9. *The impact of IPTp interventions in pregnant women in reducing susceptibility and also at recovery stage.*

Furthermore, the model was used to simulate different intervention scenarios which include the current standard of care (IPTp + ITNs), scaling strategies combining interventions at different uptake levels and enhanced ANC attendance with intervention coverage. In addition, the model analysis was done to identify optimal combinations of interventions to maximize impact of ANC in mitigating malaria transmission (see Figure 11 and Table 4 for the details extracted from the results obtained).

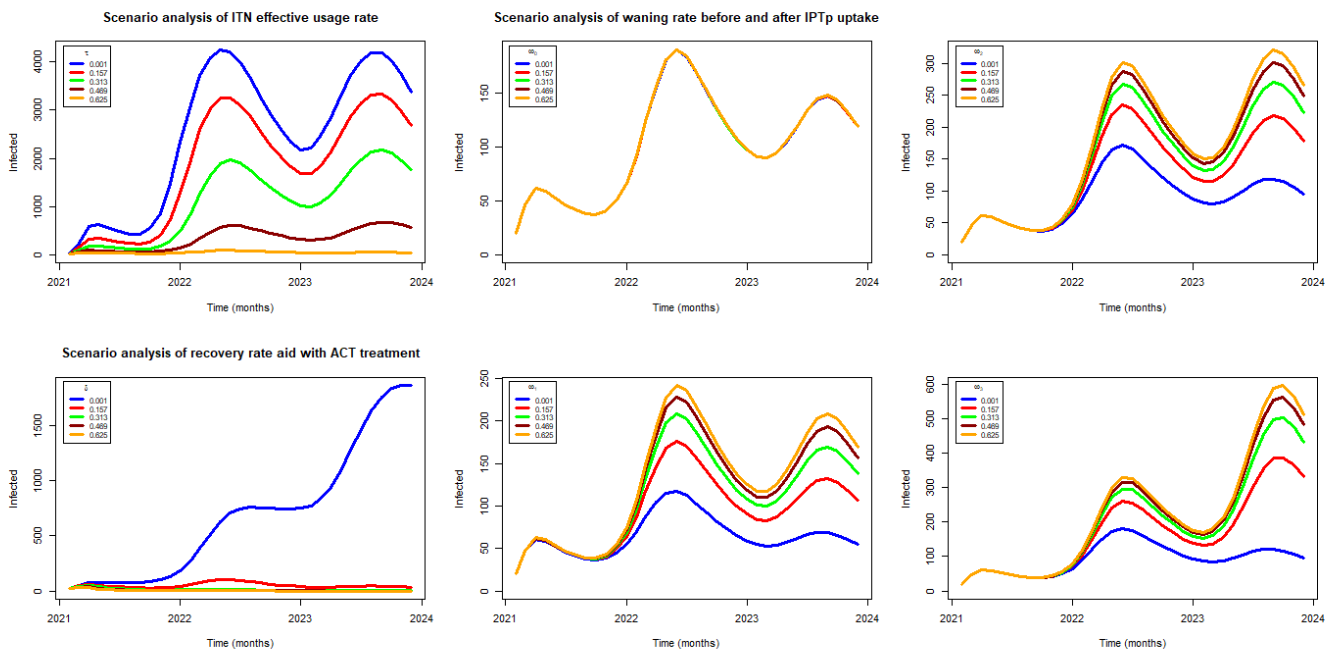

Figure 10. The impact of the various interventions (ITN, antimalaria drugs, and IPTp uptake at different dosage) on the disease dynamics at different scale.

Table 3. The total number of infected cases at different scale for the key parameters of the model.

Scale (%)	Total number of infected cases														
	Recovered transiting rate due to IPTp uptake			Effective rate of IPTp in reducing susceptibility			Susceptible transiting rate due to IPTp uptake			ITN effective usage rate	Recovery rate aided by ACT	Waning rate before and after IPTp uptake			
	ϕ_1	ϕ_2	ϕ_3	a_1	a_2	a_3	λ_1	λ_2	λ_3	τ	δ	ω_0	ω_1	ω_2	ω_3
0.1	3,591	4,311	3,701	3,603	3,662	3,699	18,452	7,962	4,803	87,075	24,107	3,577	2,279	3,205	3,336
15.7	3,589	3,597	3,569	3,255	3,476	3,466	3,810	3,612	3,452	64,642	1,748	3,584	3,337	4,533	5,870
31.3	3,587	3,283	3,523	2,937	3,299	3,245	2,479	2,924	3,199	38,332	373	3,587	3,939	5,241	6,999
46.9	3,587	3,110	3,501	2,648	3,128	3,037	2,053	2,664	3,098	11,992	182	3,588	4,307	5,658	7,576
62.5	3,586	3,002	3,488	2,386	2,965	2,842	1,836	2,526	3,037	1,843	124	3,589	4,551	5,928	7,917

Table 4. The total number of infected cases as extracted at different Intervention Scale.

	Interventions	Value (%)	Total Infected Cases
Baseline			

	Interventions	Value (%)	Total Infected Cases
	ITN	57	
	IPTp	17.1	3,337
	ACT	11	
Singly			
	ITN	62.5	1,742
	IPTp	31.3	1,707
	ACT	15.7	1,638
Mixed			
ITN + IPTp	ITN	62.5	
	IPTp	31.3	1,046
IPTp + ACT	IPTp	31.3	
	ACT	15.7	916
ITN + ACT	ITN	62.5	
	ACT	15.7	908
ITN + IPTp + ACT	ITN	62.5	
	IPTp	31.3	
	ACT	15.7	598

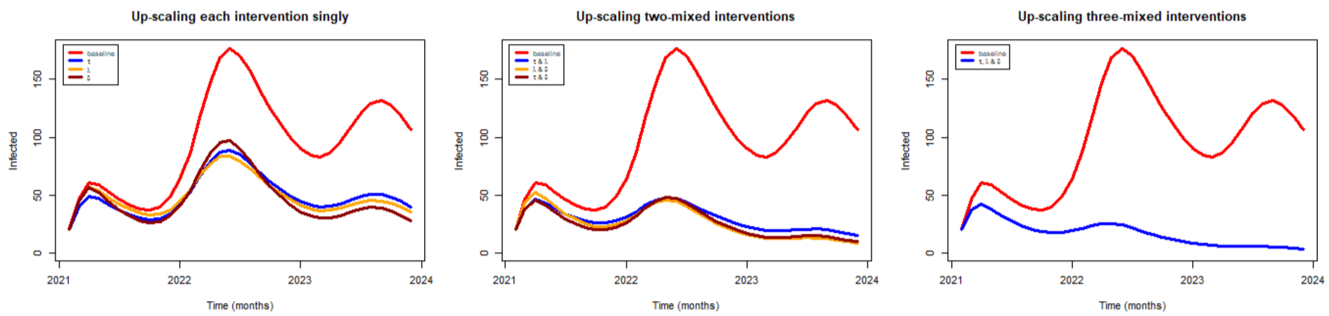

Figure 11. *The impact of the various intervention mixes at different scales on the disease dynamics.*

4. Discussion

This research work evaluated the impact of antenatal care (ANC) on the transmission dynamics of malaria infection in pregnancy. The study considered Makurdi, Benue State as the study area due to the severity of malaria incidence cases in pregnancy from 2021 to 2023 as recorded in DHIS-2 account. The data collected from the DHIS-2 platform were analyzed via the application of a deterministic mathematical model developed to study the transmission dynamics of malaria among pregnant women and to evaluate the impact of intervention uptake during ANC visit in mitigating the spread of malaria infection.

Geospatial map was used to study and convey pictorially the results of the data extracted from our source file (DHIS-2) for malaria cases in pregnant women across the 23 LGAs of Benue State. The outcome as captured in Figure 3 makes it easier to understand the spread across LGAs, to identify those with higher incidence cases and those with lower records of malaria cases. The map clearly shows that Obi, Gboko and Logo LGAs recorded the highest cumulative malaria cases between 2021 and 2023 while Makurdi recorded the highest total severe malaria cases in pregnant women within the study period.

In addition to the total number of malaria incidence and severe cases, Figure 3 also captured the map of Benue State showing the various malaria intervention coverage in pregnancy. That is, the result in Figure 3 indicates the coverage result for the treatment of malaria cases in pregnancy during

ANC with ACT intervention (which seems to be at the same measure with the total number of malaria cases recorded), the total percentage of IPTp-1, IPTp-2 and IPTp-3 uptake by pregnant women during ANC visit across the 23 LGAs of Benue State. The results show that the total percentage of IPTp uptake seems to be declining across the 23 LGAs. The first dose of IPTp uptake recorded the highest percentage of coverage with a total average of 67.7% uptake. There was significant drop in the second and third doses of IPTp uptake which recorded total average of 50.8% and 30.9% uptake respectively. This result, portrays that pregnant women were more positive and proactive to the first dose of IPTp uptake during ANC visit than the subsequent doses. Their attitude and actions pose great concern and thereby necessitate the need for monitoring intervention and evaluation for further research study in order to salvage the situation.

The values of the total number of cases and malaria infection interventions were extracted from DHIS-2 for pregnant women in Makurdi LGA of Benue State. The yearly and monthly results are represented in a bar chart shown in Figure 4 and the time series plot in Figure 5 respectively. The outcome indicated that the administration of IPTp doses witness monthly increment within each year, that is from 2021 to 2023 though the total yearly value of IPTp uptake declined across board. The results are clearly shown in Figures 4 and 5 respectively.

The mathematical model developed consists of structured compartments accounting for the various malaria preventive interventions in pregnancy and the uptake of IPTp at different dose intervals (first, second and third). The analytical evaluation of the model at equilibrium state gave two steady states: the disease-free and endemic steady states. The analysis of the model equation at the disease-free equilibrium steady state via the next-generation matrix gave the expression for the effective reproduction number.

The data obtained from DHIS-2 was used to carry out numerical simulation with the model equation and fitted some of the model parameters that were unknown. This was done using the Non-linear Least Squares Method (nlsLM) provided by the RStudio in R programming software. The details of the initial state variables and parameter values obtained from secondary sources along with the fitted curve output as earlier stated are recorded in Table 1.

The numerical simulation of the equation for the effective reproduction number (equation (5)) using the parameter values obtained in Table 1 gave a value of $R_e = 0.403$, which implies that $R_e < 1$. Consequently, the result indicates that with malaria interventions, the number of secondary infections will fade off gradually thus the disease will eventually die out of the population with time. The effective reproduction number as defined in equation (5) was further used to carry out the sensitivity analysis of some key model parameters (β, β_v, Λ_v, λ, τ, α, δ, ω and ϕ) using the expression defined in equation (6). This was done to determine their impact on the transmission dynamics of malaria infection over time among the study population.

In Table 2, the total number of incidence cases obtained from DHIS-2 for pregnant women within the study period was compared with the result for the total number of cases simulated from the fitted curve. The outcome shows a very close estimation of the actual with the fitted curve having a correlation value of 74.5%. The output of the fitted curve was further used to generate the numerical simulation of the model equation which gave the dynamics of the spread of malaria infection in pregnant women between 2021 and 2023 in Makurdi LGA. The result in Figure 7 displays the fitted result using the Non-linear Least Squares Method, the dynamics for the infected cases before IPTp uptake and the number of cases after first, second and third dose of IPTp uptake respectively.

The results show decline in the number of infected cases after each dose of IPTp indicating the significance of IPTp uptake at each stage of administrating the IPTp doses in pregnancy. Before the uptake of IPTp-1, the infected cases were controlled through the impact of other interventions to 43.1% relative to the number of the susceptible pregnant women while after the IPTp-1 uptake the percentage of infected cases obtained relatively to the susceptible population reduced to 38.3%. Similarly, after IPTp-2 and IPTp-3 the percentage were 38.7% and 31.5% respectively. Indicating a decline from 43.1% to 31.5% total infected cases of malaria in pregnancy with the complete three doses of IPTp uptake during ANC visit.

The result for the sensitivity analysis shows that ITN intervention would have the highest impact in mitigating the spread of malaria infection in pregnancy as indicated in Figure 8. The outcome agrees with the results obtained by other researchers [6, 52, 53]. The next significant parameters are the administration of ACT in aiding the recovery of infected pregnant women, the effectiveness of IPTp and the impact of IPTp uptake in reducing susceptibility of pregnant women during ANC visit. In contrast, the increment in mosquito population, transmission rate of infection from mosquitoes to pregnant women and vis-à-vis, causes corresponding increment in the number of infected cases of pregnant women in Makurdi. Similarly, increase in the immunity waning rate of pregnant women will also cause a corresponding increase in the number of malaria infected cases among the population.

Furthermore, as unraveled by the result of the sensitivity analysis of the model parameters, the administration of ACT in aiding recovery from malaria infection at the different uptake of IPTp doses is not the same across board as initially assumed. The outcome in Figure 8 indicates that the administration of ACT in aiding recovery at the IPTp-3 uptake has much significant impact in reducing the number of malaria infected cases in pregnancy relatively due to the population of pregnant women transiting into the third stage. The transitions are as a result of the preventive interventions, IPTp uptake after the first and second dose respectively which provides some measure of temporary prophylactic protection against malaria infection in pregnancy.

The intervention scenarios carried out for the key parameters used in the sensitivity analysis generated the results displayed in Figures 9 and 10 which affirmed the results obtained in Figure 8. The total number of infected cases in each scenario was extracted and captured in Table 3 to give further insight on the impact of the model parameters as obtained from the outcome. The analysis for the effective usage of ITN shows that the infection rate of malaria in pregnancy would be effectively controlled at the early stage of IPTp uptake with the total number of infected cases reduced to the nearest minimum when the rate of ITN effective usage in preventing malaria infection is increased significantly among pregnant women in Makurdi.

The results of the intervention scenario analysis further brought to limelight that increasing the effectiveness of IPTp interventions, which aim at reducing susceptibility of pregnant women, generated much significant impact at the first stage, that is, during IPTp-1 uptake thus serving as a preventive measure of malaria infection in pregnancy. As such, this preventive intervention strategy should be greatly encouraged and communicated adequately to convey the message for effective implementation. Similarly, increasing the number of susceptible pregnant women transiting as a result of IPTp-1 uptake and the subsequent doses reduces susceptibility rate drastically and consequently minimizes infection. Whereas the impact of IPTp uptake after recovering from an initial infection had significant effect only at the second dose uptake.

Furthermore, increase in the waning rate of malaria immunity in pregnancy shows a corresponding increase in the total number of infected cases. Therefore, the uptake of IPTp should be strongly encouraged to increase the prophylactic protection of pregnant women. Knowing that as they lose their immunity against malaria infection, the possibility of infection rises as shown in Figure 10.

In as much as the administration of malaria preventive interventions shows significant impact in the control of malaria infection in pregnancy, the results of the intervention mixes show better results as control measures (see Figure 11 and Table 4) and agrees with existing findings from other literatures [6, 54].

5. Conclusions

Malaria contributes significantly to the major concerns in public health which include maternal and neonatal morbidity and mortality. The impact of malaria infection is high among pregnant women since they are considered more vulnerable due to their immunological changes that increases susceptibility to *Plasmodium falciparum* infections. It is obvious that the role of ANC in mitigating the impact of malaria infection cannot be overemphasized. The outcome of this study indicates that ANC can significantly influence the impact of malaria transmission among pregnant women. The results from the analysis show that increase in the various interventions have significant impact in mitigating malaria infection in pregnancy with the effective usage of ITN having the highest impact as shown by the sensitivity and scenario analysis. It reduces infectivity effectively at the early stage of IPTp uptake and minimizes the total number of malaria cases.

Furthermore, the result indicates that pregnant women are more proactive in the uptake of the first dose of IPTp (IPTP-1) during ANC than the subsequent doses with an average total of 67.7% uptake at first stage, 50.8% uptake at the second stage and 30.9% at the third stage of uptake. The administration of ACT in aiding recovery is much at IPTp-3 uptake which could be relatively due to the population of pregnant women transiting to the third stage as a result of IPTp-1 and IPTp-2 uptake. Generally, IPTp intervention shows significant impact in reducing susceptibility consequently reducing the number of infected cases among pregnant women over time. The percentage of infected cases relative to the susceptible population was reduced within the study period from 43.1% to 38.3%, 38.7% and 31.5% at the various stages of IPTp-1, IPTp-2 and IPTp-3 respectively.

The preventive interventions for malaria infection should be strongly encouraged, especially ITN effective usage and IPTp-1 uptake to reduce malaria infection risk and provide some level of protection against malaria infection in pregnancy. Furthermore, in as much as singly preventive interventions show significant impact as control measures, mixed interventions generated much better outcome in mitigating and controlling malaria infection in pregnant women. Hence, it is pertinent that ITN and IPTp preventive intervention be encouraged during ANC visit at each stage with the administration of ACT whenever it is necessary in aiding the recovery of infected pregnant women. These recommendations are essential to both Makurdi environs and beyond for effective malaria control in pregnancy.

The use of compartmental modelling in this study plays significant role in providing the mathematical framework for effective understanding and optimizing ANC interventions for malaria infection among pregnant women in Makurdi. The use of local epidemiological data that were specific to the study area and population, provided a realistic scenario with valuable insights to the transmission dynamics of malaria infection among pregnant women in Makurdi, Benue State, Nigeria. In line with existing knowledge that IPTp reduces maternal malaria and the usage of ITN in pregnancy decreases malaria incidence and low birth weight, the results from this research study drive home the benefits of optimal uptake of ANC in Makurdi. Showing that ANC services are important strategic control measures in mitigating malaria infection and its' impact on pregnant women thereby significantly reducing the burden of malaria infection.

In addition, the study has contributed to the existing literatures on ANC interventions for controlling malaria infection in pregnancy using incidence and intervention data of Makurdi, Benue State and also provides information on: estimates of the current impact of ANC-based malaria interventions in Makurdi, the most effective intervention strategies for reducing malaria in pregnancy, the potential benefits of improving ANC attendance and intervention coverage, and guidance to inform policy decisions on malaria control in pregnancy in Makurdi Local Government Area of Benue State. The mathematical model developed through this research could serve as a tool for ongoing evaluation of malaria control strategies and could be adapted for other similar settings in Nigeria.

Abbreviations

ANC	Antenatal-Care
SI	Susceptible-Infected
SIRS	Susceptible-Infected-Removed-Susceptible
IPTp	Intermittent Preventive Treatment in Pregnancy
SP	Sulfadoxine-Pyrimethamine
DHIS-2	District Health Information Systems 2
ITN	Insecticide Treated Net
ACT	Artemisinin-based Combination Therapy
IRS	Indoor Residual Spraying
LGA	Local Government Area
WHO	World Health Organization
nlsLM	Non-linear Least Squares Method

Acknowledgments

Special thanks to Prof. Daprim Ogaji. the Postgraduate Coordinator in One Health and Disease Modelling at the Africa Centre of Excellence in Public Health, University of Port Harcourt, Nigeria and the Management Team of Corona Management System, Abuja, Nigeria for sponsoring my MSc programme in One Health and Disease Modelling at the University of Port Harcourt, Nigeria.

Author Contributions

Grace Omeche Agaba: Conceptualization, Data curation, Formal Analysis, Methodology, Resources, Software, Supervision, Validation, Writing – original draft, Writing – review & editing

Ifeoma Chinyere Ofurum: Conceptualization, Methodology, Validation, Writing – review & editing

Data Availability Statement

The data is available from the corresponding author upon reasonable request.

Conflicts of Interest

The authors declare no conflicts of interest.

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Biography

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Ifeoma Chinyere Ofurum is a distinguished public health lecturer at University of Port Harcourt with extensive experience in academia, health administration, and youth health services. She previously served as Principal Assistant Registrar and Health Administrator, leading sexual and reproductive health programs and coordinating malaria morbidity reporting. Holding doctoral degrees in Public Health and Community Health respectively, she specializes in sexual and reproductive health, adolescent health, and public health interventions. Dr. Ofurum teaches and supervises postgraduate and medical students, contributes to research and scholarly publishing, reviews academic journals, and actively participates in professional public health organizations focused on health advancement.

Research Field

Grace Omeche Agaba: Mathematics, Biomathematics, Numerical Analysis, Mathematical Modelling, Epidemiology.

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