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On Adverse Consequences of Malaria Drugs taken during Pregnancy on Babies' Malformation in Nigeria.

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Abstract. The jettison and unawareness of adverse effect of drugs has been alarming in Africa. Both prescribed and un-prescribed drugs possessed adverse effects that either unnoticed or ignored. Malaria is one of the most menace and parasitic infection in West Africa, especially Nigeria. The rate at which its drugs were being sold is increasing with the sprouting growth of the population with less concern about its adverse effects, especially to pregnant women and their unborn babies. A progressive extract and analysis was made to reveal the adverse effects of some prescribed malaria drugs during pregnancy on unborn babies in Nigeria.

Key words: Adverse effects; Child malformation; Logistic regression; Malaria drugs; Odd ratios.
AMS 2010 Mathematics Subject Classification : 62D05, 62J02, 62J86.

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Full English Abstract. The jettison and unawareness of adverse effect of drugs has been alarming in Africa. Both prescribed and un-prescribed drugs possessed adverse effects that either unaware or ignore. Malaria is one of the most menace and parasitic infection in West Africa especially Nigeria. The rate at which its drugs were being sold is increasing with the sprouting growth of the population. The adverse effects of malaria drugs are more complicated in pregnant women. *Malaria Operational Plan FY* in collaboration with *Nigeria Demographic Health Survey* conducted a survey on adverse effect of malaria drugs taken. A progressive extract and analysis was made to reveal the adverse effects of some common prescribed malaria drugs during pregnancy on unborn babies. The common prescribed malaria drugs to pregnant women are fansidar, chloroquine, daraprim, amodiaquine, nivaquine, and malozine. Thirty-two thousand (32,000) pregnant women within the age bracket of 19-49 that had used these drugs to treat malaria parasite during their first three trimesters made the final selection after a three multi-stage sampling. Logistic regression model was adopted as the methodology. It was bewrayed via the Odd Ratios that the likelihoods of chloroquine, nivaquine, and malozine causing child malformation were 0.589, 0.667 and 0.641 compare to chances of 0.417, 0.032, and 0.485 by fansidar, daraprim and amodiaquine respectively. Lastly, the Wald test statistic divulged that daraprim, amodiaquine, nivaquine, and malozine are significant contributors to the adverse effect of malaria drugs on unborn babies.

Résumé. (French Abstract) La non-prise en compte et l'ignorance des effets néfastes des médicaments ont été alarmants en Afrique. Les médicaments prescrits et non prescrits avaient des effets indésirables souvent ignorés. Le paludisme est l'une des infections les plus menaçantes et parasitaires en Afrique de l'Ouest, en particulier au Nigéria. Le taux de vente de ses médicaments augmente avec la croissance de la population. Les effets indésirables des médicaments antipaludiques sont plus compliqués chez les femmes enceintes. L'organisme *Malaria Operational Plan FY*, en collaboration avec *Nigeria Demographic Health Survey*, a mené une enquête sur les effets indésirables des médicaments antipaludiques. Les résultats de l'étude mettent en évidence les effets indésirables sur le fœtus de certains médicaments antipaludiques couramment prescrits pendant la grossesse. Les médicaments couramment prescrits contre le paludisme aux femmes enceintes sont la Fansidar, la chloroquine, le daraprim, l'amodiaquine, la nivaquine et la malozine. Trente-deux mille (32 000) femmes enceintes âgées de 19 à 49 ans qui avaient utilisé ces médicaments pour traiter le parasite du paludisme au cours de leurs trois premiers trimestres ont procédé à la sélection finale après un échantillonnage en trois étapes. Le modèle de régression logistique a été adopté comme méthodologie. Les rapports impairs ont montré que les probabilités de malformation infantile par la chloroquine, la nivaquine et la malozine étaient respectivement de 0,589, 0,667 et 0,641 et de 0,417, 0,032 et 0,485 respectivement par fansidar, daraprim et amodiaquine. Enfin, la statistique du test de Wald a révélé que le daraprim, l'amodiaquine, la nivaquine et la malozine sont des facteurs importants de l'effet néfaste des médicaments antipaludiques sur le fœtus.

1. Introduction

Drugs are chemical substances that alter or modify the manner at which body system works when taken-in – via ingestion, inhaling, or injection. Drugs may be harmful or helpful. Drugs are categorized as legal (prescribed drugs) and illegal (un-prescribed drugs) drugs (see Tinto *et al.* (2015); Sacoor *et al.* (2013)). The latter are chemical substances that are bewield by special agencies, centralized government owned hospitals and are illicit to be possessed by individuals. In other words, individuals/citizens are not allowed to be in possession of such kind of chemical substances not alone of using them. The former are legal substances if prescribed or recommended by medical practitioners to have them as medicine. Drugs do serve as healing chemical substances to treat or cure illnesses and diseases while it can also serve as recreational stimulants. Some people use drugs in other to boast their energy or to stay wide-awake for a certain period. However, drugs are also used as stimulants; such drugs are caffeine, codeine, tramadol ($C_{16}H_{25}NO_2$) etc. (see Narkowicz *et al.* (2012)).

In a similar vein, the abnormalities of structure, function, or body metabolism that is present at birth or after birth could be regarded as child malformation. Major child malformations are the abnormalities that lead to developmental or physical disabilities. Child malformations due to drugs taken during pregnancy include cecity, deafness, eyeing-impaired, hearing-impaired and misshape of any part of the body (see Kourtis (2014)). Parents of children or babies with disabilities and dis-formalities do put forward, "why my baby"? For some parents, an educative response will enable them to understand the disorder, cause, prevention, cure, and prevent future occurrences. According to World Health Organization (WHO) and Fonseca and Ferro (2013), 85 percent of children/babies encumber and handicaps are directly or indirectly via consequences of drugs, substances taking in via inhalation, direct feeding or breast-feeding from their mothers. However, of all the forms of in-take either directly by the babies (unborn and born ones) or indirectly from the mothers (or pregnant ones), drugs are the inevitable substances or in-take to cure or prevent illnesses, ailments, diseases etc. but with great side effects or consequences (see Garner and Gülmezoglu (2009); Royal College of Obstetricians and Gynecologists (2014)).

Some medications and drugs (prescribed and un-prescribed drugs) taken during pregnancy adversely hamper the growth of embryo. During gestation, almost all drugs across the placenta affect the unborn baby positively or otherwise. It is clear that women who engage in consumption of any prescribed and un-prescribed drug during pregnancy may be at risk of complications, premature labor, deformed babies and delivery problems. Drugs commonly associated with fetal malformation and structural malformation of the unborn baby include un-prescribed medications, alcohol, cocaine, tobacco, heroin and narcotics, inhalants, marijuana and many more (see Briggs *et al.* (2005); Moore *et al.* (2016)).

According to the Nigeria Demographic Health Survey (2008) and Nigeria Demographic Health Survey (2013), approximately one third of women who engage themselves in alcohol and cocaine during pregnancy consanguineous of babies with birth defects due to of alcohol consumption by mothers during pregnancy. This is referred to as visible spectrum handicap, which may include mental slowness or aberrations and emotionlessness, misshapen limbs, dwindle head, pre-natal and post-natal problems with speech and thinking impairment, narrow and small eyes openings, undersized jaw and upper lip, and congenital disorder. Therefore, the intensity of child abnormal formation relies on the frequent in-take of alcohol, if consumed during gravidity and whether it was taken excessively during the period of pregnancy. However, no considerate amount, volumes, bottles, or in-take level has been established for safe consumption; temperate or infrequent interval consumption might expose the fetus to risk. Due to this, doctors do emphatically warn to refrain from consumption of alcohol during the entire period of gravidity (see Rogers (2009)).

Plotka *et al.* (2014) also affirmed that inhalation of tobacco and marijuana especially at the first two stages of trimester endangers the fetus via possible fatal expulsion from the womb before time. The inhalation of these chemical substances might also decimate the needed amount of nutrients and oxygen rapid growth of the fetal. Nose-candy otherwise known as cocaine is a powerful stimulant for the cerebrospinal axis. If used during pregnancy, it has the power of subduing mothers' appetency as well as the severe slothing on their bodies. This could lead to blood clothing, high rate of heartbeats and assurgent blood pressure. This suppression could hamper the development of the fetus via spontaneous termination of the pregnancy. When heavy narcotics are constantly used, it can also increase the danger of premature as well as with problems of insufficient breathe in, glucose and fructose. The inhalation effects of marijuana by pregnant women are less pronounce because marijuana is one of the essential ingredients that made-up drugs in its appropriate quantity and volume (see Briggs (2001)). The more the frequent use of drugs or medications, the higher the likelihood of experiencing or expose to the risk of side effects. Wrong timing use of these chemical substances during gravidity may trigger or influence the related side effect of the drug. Some prescriptions may contain two or more drugs' composition that might lead to higher number of risks or side effects, because one drug alone may have its own adverse consequence(s) not alone of exploding adverse effects when drugs of more compositions are used (see Gray *et al.* (2011)).

No doubt, larger parts of prescribed drugs during gravidity are substantive for wellness of the unborn baby as well as its mother but the possibility of supernumerary drugs cannot the ruled out in the process. In addition, inhale substances, such as methylbenzene (toluene), phenyl methane etc. have been widely linked to congenital disorder. These mentioned solvents are contained in adhesive, paints, gelatins etc. They seemed to maintain the same negative effects as that of alcohol to pregnant women.

Poor nutritional deficiencies can also result in feeble body weight growth of both unborn and newly born babies. Aberrations via comestible defects such as mindset illness, composure defects are miniature in the entire stages of pregnancy compare to defects from oral consumable chemical substances. However, some food preservation substances and additives like saccharin, colourings, Red 2, margarine, and salt might endanger the fetus especially during the first stage of trimester (see Al-Saleh *et al.* (2011)). It was because of this that the Nigeria Medical Association disallowed the use of Red 2 due to its contingency of causing cancer and possibility of weakening the fetal tissue.

Additionally, men were also cautioned to deviate from using medications before sex so as not to damage their sperms and distort genetic contents that could lead to birth defects (see Dejmek *et al.* (2002)). Pregnant women have been advised by Nigeria Demographic Health Survey (2003) and NDHS (2008) to take extra precautions on substances like antibiotics, alcohol, cocaine, steroids, gentamycin, kanamycin, neomycin, cigarette and other drugs that the WHO have warned to stay away from during pregnancy.

Having said this, malaria being another threatening, most spread and parasitic infection among pregnant women. It is caused by the parasite known as plasmodium falciparum, a harm type of mosquitoes. It is an infection common among three continents – Africa (especially West Africa), Asia and South America (see Pem *et al.* (2016)). Its symptoms range from high body temperature, headache, joint pains, weakness, fever. It might cause nausea, vomiting, mood swing, unconsciousness, hamper the growth of the unborn baby and miscarriage in pregnant women when exposed to bites of the malaria caused mosquitoes within the first three trimesters.

To measure the adverse effects of the most common six (6) malaria drugs taken during pregnancy in Nigeria, tetanus injection before birth, and iron tablets /syrup drugs taken during pregnancy on unborn babies, a survey analysis will be carried out on the of 30,000 trials of pregnant women in Nigeria during their first three trimesters. Malaria Operational Plan FY, 2016 in collaboration with NDHS, conducted the survey. In the light of the above, we want to examine whether previously reported associations and relationships between malaria drugs taken during pregnancy and the effects of these drugs on child malformation or deformation could be confirmed and to explore whether new associations might be identified.

The sections in this survey report will be structured as follows: The second exhibits literature on related surveys, analysis, deductions as regards the adverse effects of malaria drugs taken during pregnancy on unborn babies. The third section pinpoints the methodology to be used. The fourth section entails the results and discussion of analyzes, while the fifth section gives conclusion as well as recommendations.

2. Literature Review

Drugs can have different side effects on the health of pregnant women. Side effects of drugs, such as tobacco and highly ethanol contain solutions are being the direct cause of death to some people year-in-year-out, while some planted drugs like hemp, marijuana and shrooms cannot lead to cessation of life.
According to the NDHS (2013), about 150,000 babies are born with malformation each year in Nigeria due to drugs taken by their mother during pregnancy. However, at times, some drugs do not necessarily terminate life but their accumulation of side effects might lead to stoppage of the heartbeat. Persons experiencing side effects of drug(s) are referred to as addictive users or intoxicants. These users might want the experience in terms of additional stimulant or unwanted and unknown adverse consequences; such adverse effects may cause structural malformation or malfunction of some part of their body.

Major structural malformations are usually emanated from the stage after the fertilization of the egg that precedes the development into fetus, usually within the first seven weeks. These weeks are for metamorphosis formation after the development of the fetus, with higher likelihood of being distort, halt, and abuse by the aforementioned chemical or planted substances sourcing the unborn babies' malformation right from the fetus.

It has been reported that the number of drugs inducing physical malformation keep increasing yearly. According to the NDHS (2008 and 2013), there has been an incremental from one to three percent to two to three percent yearly of deformation of babies right from the metamorphosis due the adverse consequences of drugs. Remnants of drugs in pregnant women would in no doubt find its way into the fetus by the period babies are changing form inside their mothers. By doing so, the embryos would react to drugs and it side effects in the manner with the carriers (mothers). Any class of chemical substances or drugs that reduces pains induces sleep and that serve as mood alteration have been identified for downbearing the relative of inhaling and exhaling when in large quantity and frequently. There is high possibility of the carrier's blood circulating into the baby's blood stream and the baby experiencing the same difficulties as the mother. Additionally, the measured portion at the recommended time and the intrinsic degree to which the toxic substances or drugs harm the fetus define the strained reaction by the infant.

Mohn *et al.* (2018) maintained that aspirin side effects have the high chance solidified mass of blood, heart failure, and congenital disorder. They revealed that, ephedrine might cause heart-rate problems and birth defects. In a similar vein, Douglas *et al.* (2011) revealed that the adverse effects of crystalline alkaloid and pethidine might lead to miscarriage, atypical sprout, deformed limbs, small head, prenatal and postnatal problems, and congenital malformations on the unborn baby. They also disclosed that constant use of acetaminophen exposes infants to kidney instability.

Tamuno *et al.* (2011) in their study on the effects of drugs taken during pregnancy on child malformation in Kano, Nigeria reveals that the persistent in-take of antibiotics during pregnancy may harm a growing fetus. They stressed further that constant use of tetracycline during gravidity could sprain and deformed bones on the unborn baby while persistent use of gentamycin, kanamycin, neomycin, and streptomycin (all brand of mycin) may cause deafness on the unborn babies. NDHS (2008) disclosed that some prescribed and legit drugs could be harmful to infants. They emphasized further that several closely related fat-soluble vitamins such as retinol might cause medical disorders at birth — deafness and blindness; and that goitrogen substances have the high the possibility of resulting into enlargement of the neck and secretion of excessive production of thyroid hormone in infants.

Below are some examples of malaria drugs that may cause malformation on unborn baby according to WHO (2011).

- Chloroquine and Amodiaquine that are used in treating red pimples adversely result in disabilities/deformation in the transformation of stage-to-stage development of the fetus.
- Daraprim brands, such as anticonvulsant and carbamazepine that are used to subdue anticipation of epilepsy are usually accompanying with congestive heart failure, facial pimples, and instability of mentality in unborn babies.
- Drugs for preventing or acting against migraines, for example, hemicrama, enxaqueca are characterized with poor coordination and decreased muscle tone on the unborn child.
- Analgesic, anodyne, as well as anti-inflammatory drugs that o not contain steroids usually increases thrombus in pregnant women as well as shortening of the labour stimulant hormones.
- Drugs for preventing coagulant, such as Coumadin for treating of cardiac disease, interrupted supply of blood to the brain in pregnant women have the likelihood of damaging infants' lungs and brains. Anticoagulants are also, associated with facial malformations and mental retardation of the unborn babies.

Adverse consequences of medical prescribed in-takes boils down to the kind of in-takes, the dose, the frequently use, rate of dissolve into the body, what other drugs used concurrently. Differences in adverse consequences are due to body chemistry, immunity, and body tolerance. Additionally, ethanoic contained solutions; cigarette and un-prescribed drugs would definitely be great risk to pregnant women and their unborn babies. According to Pem *et al.* (2016), if possible, pregnant women should do everything at their disposal to avoid being bitten by mosquitoes to distance themselves from malaria drugs because as any anti-malarial agent passes through the placenta it causes haemolytic anaemia in neonates. Its adverse effect might affect the colour of the placenta and possibly risk the change in complexion of the on-going growth of the fruit of the womb. The Royal College of Obstetricians and Gynecologists (2014) stressed that the usual pharmacological adverse of anti-malaria agents are nausea and diarrhea.

They further affirmed that the constant discharge of water from the bowel of the pregnant mothers might reduce the watery fluid surrounded by the placenta to dry it instead of constant moisture.

Given the high magnitude, unawareness and relevancy of the side effect of malaria drugs to pregnant women especially in West Africa countries, it is due to this that each country constituted demographic health agencies for periodical embarking of health related surveys. Reviewing and carving-out hidden facts about adverse effects of drugs, abuse of drugs, circulation of contraband drugs etc. However, it is noted that less attention has been given to adverse effect of malaria drugs and some iron tablets/syrup taken by mothers during pregnancy. Due to this, extracts/information made from the comprehensive survey made by Malaria Operational Plan FY, 2016 in collaboration with Nigeria Demographic Health Survey (NDHS), Nigeria Population Commission (NPC) and United States Agency for International Development (USAID).

The extract is to ascertain and explore the relationship between the use of malaria drugs taken during pregnancy on children malformation; to form a model that would help to reveal the consequences or adverse effects of some prescribed malaria drug(s) taken during pregnancy on child malformation. Lastly, to test the overall significance of individual prescribed malaria drugs to know if the co-variates (drugs taken during pregnancy) have significant relationship with the malformation of the born child (regressant).

3. Methodology

Logistic regression will be used as the ideal statistical model because it is a type of regression model in describing response variable (conducting clinical trials) that is binary or dichotomous in nature based on predictors (explanatory variables) that can any form of the scale of measurements (Nominal, ordinal, interval or ratio scale). The predictors to be used in this study follow the nominal form of measurement. The power of attaching probabilities (predictions) to dichotomous outcomes makes the regression type model befitted model to assess the contribution of each predictor.

Logistic regression otherwise called the logistic model is a type of regression model for foretelling the outcome of binary responses, that is variable with mutually exclusive condition of only two possible outcomes, for example "on" or "off"; "female" or "male" (gender); "true" or "false"; "yes" or "no"; "presence" or "absence" of a signal founded on a dichotomous dependent variable. Its target is to miniature the chance of the bi-outcomes via a linear transfer function (otherwise known as logit link function) of the dependent variables. (see Gujarati (2004); Cox (2010); Pindyck and Rubinfeld (2005)). Moreover, it could be a bi- or multinomial logistic regression — the formal is for binary (Bernoulli or dichotomous trials) coded outcomes while the latter is for more than two (multi-) coded outcomes. It uses the log-odd of the favorable outcomes (e.g. yes, true etc.), that is the probability

of the logit to fit the regressors via the linear regression such that the Odd Ratio (OR) is use to access the magnitude effect in the regression. In other words, OR estimate and compare the odd that belong to a group with the case outcome of such group (see Adrich and Nelson (1995); Krammer (1991)).

Let Y be the two possible dependent random variable with its regressors $Z_1, Z_2, \cdots\cdots, Z_i$, then the linear multiple regression line is written as:

$$Y = \beta_o + \beta_1 Z_1 + \beta_2 Z_2 + \cdots\cdots + \beta_i Z_i \tag{1}$$

The linear transfer function, which is the logit (probability of the logit) link function for the probability of one of the dichotomous outcomes of the dependent variable say "π" for the bi- logistic regression is as follow:

$$h(z) = \ln\left(\frac{\pi(z)}{1-\pi(z)}\right) = \beta_o + \beta_1 Z_1 + \beta_2 Z_2 + \cdots\cdots + \beta_i Z_i \tag{2}$$

or

$$\frac{\pi(z)}{1-\pi(z)} = \exp\left(\beta_o + \beta_1 Z_1 + \beta_2 Z_2 + \cdots\cdots + \beta_i Z_i\right) \tag{3}$$

is the Odd Ratio, where

$$\pi(z) = \frac{\exp\left(\beta_o + \beta_1 Z_1 + \beta_2 Z_2 + \cdots\cdots + \beta_i Z_i\right)}{1 + \exp\left(\beta_o + \beta_1 Z_1 + \beta_2 Z_2 + \cdots\cdots + \beta_i Z_i\right)} = \frac{1}{\exp\left(\beta_o + \beta_1 Z_1 + \beta_2 Z_2 + \cdots\cdots + \beta_i Z_i\right)} \tag{4}$$

where β_0 is known as the intercept; $\beta_1, \beta_2, \beta_3, \cdots\cdots, \beta_i$ are called the slopes (regression coefficients) of $Z_1, Z_2, Z_3, \cdots\cdots, Z_i$ respectively. Unlike the models with stringent assumption of normality, multiple logistic regression is associated with non-normal error term, dichotomous trial constraint on response function and non-constant error variance.
To assess the contribution of individual predictors in the multiple logistic regression models, the Wald test statistic will be employed. It is the ratio of the square of the slope to the square of the standard error of the slope. It makes use of the chi-square distribution as its asymptotical distribution.

$$WA_i = \frac{\beta_i^2}{(S.E)^2_{\beta_i}} \tag{5}$$

The Nagelkerke-R^2, Cox and Snell R-square and the Likelihood Ratio tests will be used to assess goodness of fit: as it represents the proportion of variance in the criterion that is explained by the predictors (see Demaris (1992)).

4. Data Presentation and Analysis

The availability of accurate data is essential for deriving reliable result and for making accurate decisions in any research work. The data used in this project are secondary data; they were collected from the Malaria Operational Plan FY, 2016 under the President's Malaria Initiative (PMI), an initiative oversaw by National Anti-malarial Treatment Policy (NATP) under the federal ministry of health national malaria and vector division, Abuja, Nigeria. It was also collaborated by NDHS, NPC and USAID. The PMI designed questionnaires and administered it to population of pregnant women within the age bracket (19-49), who gave birth a month ago at the time of the survey. The survey was conducted in 2017 after a successful pilot survey in 2016. The population covered was the population of all pregnant women in Nigeria within the age bracket of 19-49. Firstly, the target population, Nigeria was divided into 36 states including the Federal Capital Territory (FCT). Each state was sub-divided into Local Government Area (LGA) unit and each LGA was sub-divided into localities, each locality was subdivided into Enumeration Areas (EAs). The lists of approximately 212,080 EAs with 7,864 households were evaluated as sample frame.

A probability sample was used in selecting households and all women in the age bracket (15-49) identified in the households were eligible to be interviewed. Furthermore, sub-sample of one-third of the household selected for the survey. Finally, household survey was conducted on about 32,000 pregnant women within the age bracket of 19-49 that had used treated malaria parasite to during their first three trimesters. While 2000 of these pregnant women failed to response (that is non-response). Questions were asked from six (6) known prescribed malaria drugs; fansidar, chloroquine, daraprim, amodiaquine, nivaquine and malozine and unknown prescribed malaria drugs as well as tetanus injection before birth and iron tablets /syrup used during pregnant.

The co-variates are :

- *Tetanus injection* given before birth: score was recorded to be: 0 = no, yes= 1, and denoted as Var. 1.
- During pregnancy, given or bought *iron tablets /syrup*: score was recorded to be: 0 = no, yes= 1, and denoted as Var. 2.
- During pregnancy, *had difficulty with day light vision*: score was recorded to be: 0 = no, yes= 1, and denoted as Var. 3.
- During pregnancy, took *fansidar* for malaria: score was recorded to be: 0 = no, yes= 1, and denoted as Var. 4.
- During pregnancy, took *chloroquine* for malaria: score was recorded to be: 0 = no, yes= 1, and to be denoted as Var. 5.
- During pregnancy, took *unknown malaria drug*: score was recorded to be; 0 = no, yes= 1, and denoted as Var. 6.
- During pregnancy, took *daraprim* for malaria: score was recorded to be: 0 = no, yes= 1, and denoted as Var. 7.

- During pregnancy, took *amodiaquine* for malaria: score was recorded to be: 0 = no, yes= 1, and denoted as Var. 8.
- During pregnancy, took *nivaquine* for malaria: score was recorded to be: 0 = no, yes= 1, and denoted as Var.9
- During pregnancy, took *malozine* for malaria: score was recorded to be: 0 = no, yes= 1, and denoted as Var. 10.
- During pregnancy, took *no drug malaria taken*: score was recorded to be: 0 = no, yes= 1, and denoted as Var. 11.

Table 1. Descriptive statistics

Child malformed	$\%ofyes$"1"	$\%ofNo$"0"	Mean	Skewness	Kurtosis
–	89.2	9.7	34.5	35.01	30.145

Table 1 (page 627) consist of dependent variable or response variable descriptive statistics, having categories (child was malformed due to the malaria drugs taken by pregnant women during pregnancy which was coded "1" versus child was not malformed due to the drugs taken by pregnant women during pregnancy) coded "0". The co-variates; "pregnant women took injection before birth", "pregnant women gave or bought iron tablets/syrup", "during pregnancy, had difficulty with day light vision", "took fansidar for malaria during pregnancy ", "took chloroquine for malaria during pregnancy, took unknown malaria drug during pregnant ", "took daraprim for malaria during pregnancy", took amodiaquine for malaria during, "took nivaquine for malaria during pregnancy", "took malozine for malaria during pregnancy ", "during pregnancy took other drug for malaria ", "during pregnancy took no drug for malaria".

According to output, for each or combination of the co-variates (i.e., for each or combination of the malaria drugs used), 89.2% cases of child malformation due to those malaria drugs listed above taken by their mothers during pregnancy were recorded and 9.7% cases were not malformed due to those malaria drugs listed taken by their mothers during pregnancy. The mean of children that were malformed due to the malaria drugs taken by their mothers was 34.5. In addition, the skewness was calculated and it was positively skewed with 35.01 and kurtosis estimated to be 30.145.

Table 2. The Logistic Regression Coefficients

Variables	β_i	S.E	Wald	Sig.	Odd Ratio	95% Lower C.I	95% Upper C.I
Tetanus injection	0.039	0.070	0.312	0.576	1.040	0.907	1.191
iron tablets /syrup	0.234	0.007	0.082	0.774	1.000	0.999	1.001
light vision	-0.055	0.128	0.185	0.667	0.947	0.737	1.215
fansidar	0.359	0.743	0.233	0.000	1.432	0.333	6.147
chloroquine	-0.043	0.439	0.010	0.922	0.958	0.405	2.264
unknown malaria drug	-0.392	0.371	1.117	0.291	0.675	0.326	1.398
daraprim	0.335	0.393	0.728	0.022	0.715	0.331	1.545
amodiaquine	3.375	1.545	4.770	0.029	0.034	0.002	0.707
nivaquine	3.345	2.044	2.679	0.102	28.375	0.517	1558.14
malozine	0.581	1.072	0.293	0.021	1.787	0.219	14.609
no drug malaria taken	-0.313	0.364	0.738	0.390	0.732	0.210	6.826
regression coefficient	2.844	0.367	59.988	0.000	17.178	–	–

Keys: S.E=Standard Error; Sig.=Significance; C.I= Confidence Interval.

Table 3. Odd Ratio Coefficients and its Interpretation

Prob.	Tet. Inj	iron tab.	light vis.	fan.	chlo.	um.	dar.	amo.	niva.	malo.	ndmt
π_i	0.409	0.500	0.485	0.589	0.496	0.403	0.417	0.032	0.967	0.641	0.545
95% Lower C.I	0.201	0.324	0.254	0.350	0.238	0.209	0.222	0.014	0.746	0.457	0.332
95% Upper C.I	0.562	0.691	0.628	0.693	0.579	0.548	0.517	0.041	1.218	0.806	0.704
P-values	0.002	0.001	0.030	0.000	0.010	0.003	0.055	0.045	0.023	0.000	0.311

Tet. Inj =Tetanus injection; iron tab.=iron tablets;
light vis.=light vision; fan.=fansidar; chlo.=chloroquine;
um.= unknown malaria drug; dar.=daraprim; amo.= amodiaquine;
niva.= nivaquine; malo.=malozine; ndmt=no drug malaria taken.

The Binary logit model with main effects of these predictor variables, that is the prediction equation fitted using coefficient estimates in Table 2 (page 628) is ;

Y=logit(π) = 2.844 + 0.039 (Tetanus injection) + (iron tablets /syrup) - 0.055 (light vision) + 0.359 (fansidar) + 0.043 (chloroquine) + 0.392 (unknown malaria drug) + 0.335 (daraprim) + 3.375 (amodiaquine) + 0.581 (nivaquine) + 0.181 (malozine) - 0.313 (no drug malaria taken),

where π denote the probability of the mean response of a child being malformed due the adverse effect of malaria drugs taken by his/her mother during pregnancy. The dependent variable, Y = child malformed, child malformed due to the effect of malaria drugs taken during pregnancy by his/her mother = 1, child not malformed due to the effect of malaria drugs taken during pregnancy by his/her mother = 0. This implies that the mean response of Y is the probability of a child being malformed due adverse effect of malaria drugs taken by his/her mother during pregnancy. The malaria/syrup drugs used were called the co-variates Tetanus injection, iron tablets /syrup, $\cdots\cdots$ no drug malaria taken.

The estimates of each predictor in Table 2 (page 628) gives the information about the contribution or importance of each of the predictor $\widehat{\beta}$ values whether positive or negative tells us about the direction of the relationship (which factors increase the likelihood of a yes answer and which factors decrease it). $\widehat{\beta}$ indicates that an increase in the independent variable score will result in a decreased probability of the case of recording a score of one in the dependent variable. However, the $\widehat{\beta}$ value for, had difficulty with day light vision" which is -0.055, indicates that the more difficulties had during pregnancy, the less likely it is that there will be report child malformation. The $\widehat{\beta}$ value for chloroquine taken for malaria which is -0.043, it suggests that chloroquine for treating malaria during pregnancy does not has adverse effect on the unborn babies. Additionally, the $\widehat{\beta}$ value for took un-prescribed drug for malaria which is -0.392 does not contribute to adverse effect child being malformed due to their mothers taken it during pregnancy. Whereas, positive values of $\widehat{\beta}_s$ for tetanus injection taken before birth, took fansidar for malaria during pregnancy, daraprim took for malaria during pregnancy, amodiaquine took for malaria during pregnancy, nivaquine took for malaria during pregnancy, malozine, took for malaria during pregnancy and took other drugs for malaria during pregnancy contributed or more likely to answer child was malformed due to the adverse effect of drugs taken during pregnancy.

4.1. Estimating the Odds Ratio

Another useful piece of information in Table 2 (page 628)is the OR = ($\exp(\widehat{\beta}_i)$). This value is for each of the independent variable; it represents the change in odds of being in one of the categories of outcome when the value of a predictor increases by one unit. The odds ratio for "tetanus injection took before birth" which is 1.040, its greater than one indicates the more tetanus injection taken during pregnancy

the more likely to report a case of child malformation, the OR for "fansidar taken during pregnancy" which is 1.432 and greater than one, the more likely to caused child malformation, the odd for "during pregnancy took or given iron tablets/syrup which is (1.000) is inconclusive because one is the border line that determines likely to increase or decrease of an effect when some units are added. Furthermore, the ORs of "malozine, nivaquine and took other malaria drug during pregnancy" which are 1.787, 28.375 and 1.199 respectively are greater than one, are likely or have higher chances to caused child malformation due to their adverse effect. It is to be noted that the chance of Nivaquine causing malformation on unborn child is very high due to its odd ratio being extremely high. While the Odds ratios for (Amodiaquine, daraprim, chloroquine and unknown drug for malaria) which are 0.034, 0.715 and 0.675 respectively are less than one indicates less likely report of child malformation when taken during pregnancy. Also, for each of the OR $\exp(\widehat{\beta}_i)$ shown in Table 2 (page 628) above, there is a 95 percent confidence interval (95% C.I for $\exp(\widehat{\beta}_i)$) displayed giving a lower value and upper value.

4.2. Prediction of Probabilities

Probabilities can be predicted using the estimated odds from the logit model is given by

$$\pi_i = \frac{Odd}{1 - Odd}$$

(Tetanus injection) + (iron tablets /syrup) - 0.055 (light vision) + 0.359 fansidar + 0.043 chloroquine + 0.392 (unknown malaria drug) + 0.335 daraprim + 3.375 amodiaquine + 0.581 nivaquine + 0.181 malozine - 0.313 (no drug malaria taken). It implies that there is 0.409, 0.500, 0.485, 0.589, 0.496 chances of tetanus injection, iron tablets /syrup, had difficulty during day light vision, fansidar, and chloroquine taken before birth causing child malformation respectively. While the likelihood unknown malaria drug during pregnant, daraprim, amodiaquine, nivaquine, no drug for malaria took and malozine causing child malformation by their mothers in taken are 0.403, 0.417, 0.032, 0.667, 0.545 and 0.641 respectively.

4.3. Inference on the Logit Model

As earlier mentioned the Wald's statistics is simply the square of the Z-variate and this follow a χ^2-distribution with one degree of freedom. The test will be carried out at 5% level of significant.

Table 4. Test of Hypothesis using the Wald's Test Statistic

Coefficients	β_1	β_2	β_3	β_4	β_5	β_6	β_7	β_8	β_9	β_{10}
P-values	0.576	0.774	0.667	0.00	0.922	0.029	0.022	0.09	0.102	0.021

Testing the significant of each of the regression coefficient has independent to the malformation of babies. The null hypothesis for each regression of the coefficient is stated that the drug that led to the coefficient is independent of child malformation while the alternate hypothesis stated otherwise. For example, the null hypothesis for β_1 stated that tetanus injection used before birth is independent of child malformation while it alternate stated otherwise. Moreover, since the p-values = (0.576, 0.774, 0.667 and 0.922) for β_1, β_2, β_3 and β_5 respectively are strictly greater than 5% level of significant, it implies that the drugs (tetanus injection, iron tablets /syrup, light vision, and chloroquine) contributed to the coefficients are statistically insignificant. Similarly, the p-values = (0.00, 0.029, 0.022, 0.090, 0.102, 0.021) for the coefficients β_4, β_6, β_7, β_8, β_9 and β_{10} respectively are strictly less than 0.05, it connotes that fansidar, unknown malaria drugs taken by these pregnant mothers, daraprim, amodiaquine, nivaquine and malozine are significant contributors to the adverse effect of malaria drugs on unborn babies.

4.4. Test of Hypothesis using the Cox and Snell R-Square; and Nagelkerke R-Square

Here, binary logistic regression was performed to assess the impact of a number of factors on the likelihood that respondents would report that they had a problem of child malformation.

Table 5. Model Summary

Step	-2 Log-likelihood	Cox & Snell R-Square	Nagelkerke R-Square	Chi-square
-	0.372	0.261	4.161	9.34
P-values	0.002	0.000	0.009	0.004

The model as a whole explained between 37.1% (Cox and Snell R-square) and 26.2% (Nagelkerke R-square) of the variances in child was malformed due to the malaria drug(s) taken status, and correctly classified 85.1% cases. As shown in Table 5 (page 631), only five of the independent variables made a unique statistically significant contribution to the model (took fansidar for malaria, took daraprim for malaria, took amodiaquine for malaria, and took malozine for malaria).

5. Conclusion

From the antecedent, results from the study make it possible to predict the possible effect of an individual malaria drugs (fansidar, chloroquine, tetanus injection took before birth, amodiaquine, nivaquine, daraprim and malozine) taken during pregnancy on child malformation. This we believe will assist the PMI, NDHS, USAID, WHO and physicians to know which malaria drugs to recommend and prescribed to pregnant women during pregnancy because of adverse effect of drugs not only on the pregnant women but also on their unborn babies.

5.1. Recommendation

Having stressed the drugs factor in malformations and other problems of encountered by fetuses and newborns, protective and preventive measures, both pregnant women and by health professionals are of paramount and awareness. However, it is also important to keep the drug factor in proper perspective.

The great majority of malformations and other short falling of pregnancy are caused not only by drug factors but also by other crucial factors. Drug hazards should be stressed not because the ill effects are so numerous or so likely to occur, but because when they do occur they can be so devastating. In addition, in most instances, the hazards of drug use can be so easily avoided. Pregnant women who follow the precautions listed below, whose physicians use ordinary prudence in prescribing for their patients, can be assured that the risks and side effects of drugs in pregnancy will be minimized. We recommend that pregnant women, as well as the physicians should observe the following cautions:

- To try and avoid taking of any drug during pregnancy unless there is a paramount medical need for it. Pregnant women should be extremely careful especially in the first trimester of pregnancy.
- If need be for malaria drugs and other antibiotics, pregnant women should not increase or reduce dosage/timing of in-takes; discontinue usage sooner or continue it longer than directed by physicians. In addition, taking of un-prescribed drugs/medications might have the high chance of adverse effect on the unborn baby.
- All self-prescribed medications should be discontinued immediately menstrual period is missed, then, a pregnancy test or visitation to one's physician should be followed to ascertain the truthfulness of the pregnancy in other to stick with prescribed drugs.
- "Home remedy" drugs should decimate immediately pregnancy is confirmed.
- PMI, NDHS, WHO and other medical bodies should try to create awareness of adverse of malaria to drugs not only to pregnant women but also to every citizen.

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