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Drugs exposures during pregnancy and neonatal risk assessment

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Abstract

Background: Medication use is inevitable in the management of chronic or acute disease conditions during pregnancy. However, obstetric pharmacotherapy is most challenging for healthcare providers as they make effort to balance the benefit and risk of medication use during pregnancy.

Objective: To profile medical conditions and medication use during pregnancy, and to assess potential or actual neonatal risks following drug exposure in pregnancy.

Methods: The study was carried out in 6 healthcare facilities in Edo State, Nigeria. A total of 2,530 pregnant women attending antenatal clinics (ANC) in the health facilities were recruited and followed-up to delivery. Demographic, clinical, obstetric, and drug information were collected from women during their first encounter with the investigator and these data were updated in subsequent follow-up visits by the women. Data were collected through interviews, review of medical records and ANC cards. At delivery, the clinical information of the neonates was obtained and recorded and neonatal risk assessment undertaken. The prescribed medications were classified as safe, low risk and high risk drugs in pregnancy. Paired sample *t*-test method was used to copmpared categorical veriables and p-values <0.05 were considered significant.

Results: A total of 900 out of the 2,530 participants were followed up to delivery. Malaria and other infectious diseases were the most commonly encountered medical conditions, and 6,639 medication exposures during pregnancy were reported among the 2,530 participants. Most drugs were used during second and third trimesters of pregnancy. Apart from routine drugs (iron salts and multivitamins), anti-malarial drugs (55.4%, 889/1605), and antimicrobials (19.7%, 316/1605) were most commonly prescribed. Neonatal risk assessment indicated that 47.5%, 45.7% and 5% of the drug encountered were considered safe, low risk and high risk in pregnancy respectively. One congenital malformation (extra digit in the new born) was reported in the neonates.

Conclusion: The study revealed that anti-malarial drugs and antimicrobials were most frequently prescribed. Almost all prescribed drugs were either safe or of low risk in pregnancy. It was observed that drugs use during first trimester of pregnancy was low.

Keywords: drug exposure; neonatal risk, and pregnancy

Introduction

Pregnant women are routinely excluded from pre-license clinical trials for the fear of harming mother or the developing foetus. Most medicines are registered for use with limited information on their safety during pregnancy and therefore are not recommended for use by pregnant women. However, drug therapies in chronic diseases such as hypertension, diabetes, epilepsy and Human immunodeficiency virus (HIV) or other acute illness that harm the mother and the unborn child cannot be discontinued during pregnancy [1]. Hence, health care providers are expected to use drugs for pregnant women with the view to alleviate the suffering of the mother and with no harm to the unborn baby.

Consequently, many medicinal products are subject to contraindications or special warnings because they have not been sufficiently studied during pregnancy or studies in animals have revealed adverse effects on the foetus (teratogenic, foetotoxicity or other) [2]. Assessment of drug exposure during pregnancy requires collection of data on the baseline. By enrolling women as they come to ANC, detail of their medications (prescribed and non-prescribed drugs) history collected and follow–up to term where the pregnancy can be assessed. However, efforts to increase access to medicines for major diseases such as malaria, HIV/AIDS, pneumonia. Hypertension, diabetes and other diseases has accelerated. Novel life-saving therapies such as artemesinin-based combination therapies (ACTs), antiretroviral (ARVs), anti-infective and vaccines have been introduced on a large scale [3]. The safety of some of these therapies during pregnancy is unknown. In some infections (HIV/AIDS, malaria), failure to treat effectively may result in death, disease transmission or poor outcomes for the mother and/or the baby. However, the medicines themselves may cause toxicity, including birth defects. Therefore, knowledge about the risks of medicines used during each trimester of pregnancy is essential in order to assist patient management [4].

Every pregnancy has a risk of an abnormal outcome regardless of drug exposure. Reproductive toxicologists generally consider the four major manifestations of abnormal foetus development to be growth alteration, functional deficit,

structural malformation, and death [5]. The purpose of collecting and evaluating data on drug exposure during pregnancy is to assess whether a particular drug exposure can result in abnormal foetus development. Clinical classifications of pregnancy outcomes include live births, elective terminations, and foetus losses, i.e., spontaneous abortions (loss prior to 20 weeks post-conception), and foetus deaths/stillbirths (loss beyond 20 weeks post-conception) [6]. Among live births, preterm birth (before the 35th week after conception) and low birth weight (<2500 grams) are also considered adverse pregnancy outcomes occurring in 1 of 8 and 1 of 12 live births, respectively [7].

The WHO treatment guidelines for malaria and HIV/AIDS reflect these concerns about potential risk during pregnancy [8]. In practice, pregnant women in countries with high burden of infections are likely to be exposed to numerous classes of medicines since the number of pregnancies among HIV-positive women already on ARVs and other diseases is increasing in both developed and developing countries [9] and many pregnancies are unplanned. At the same time, changes in drugs delivered across the care continuum (antenatal, delivery, postpartum) pose operational challenges in high-burden low-resource settings. It has been observed that in confirmed and unconfirmed diagnoses such as malaria, the artemesinin are being used extensively without knowledge of pregnancy status in women of childbearing age. Thus the likelihood of first trimester exposures to medications has increased and is expected to increase even more [10]. Thus, study of drug exposure during pregnancy is essential.

Study of drug exposure during pregnancy is different from other post-marketing surveillance techniques in that pregnant women are enrolled before the outcome of the pregnancy is known [11]. Thereby many outcomes can be monitored. The drug exposure during Pregnancy study will provide evidence on the risk of increased prevalence of clinically important malformations at birth associated with drugs to which women might be exposed. The process is not a drug-specific; this confers substantial advantages for wider use of the same dataset. The processes builds on the fact that in most African countries 90% of women access health care during pregnancy, and malaria treatment, HIV counselling and testing and prevention from mother to child treatment (PMTCT) programmes have good links with reproductive health services. It is expected that this study will contribute to a pooled of database on safety of medications in pregnancy. This study will also serve as a surveillance system for the safety of medicines used in pregnant women.

Although there are many figures quoted for the prevalence of major congenital malformations, these are greatly dependent on the population studied, the point at which the data is collected after birth, and the classification of congenital defect (e.g. minor, major, cosmetic). About 4 percent (1/28) of babies are born each year with a major birth defect or congenital malformation [7]. For the majority of major birth defects (about 65 percent), the etiology is unknown [5]. Chemically induced birth defects, including those associated with drug exposure, probably account for less than 1 percent of all birth defects; few drugs are proven human teratogens at therapeutic doses [12]. Among thousands of drugs available, only about 20 drugs or groups of drugs (mostly being anticonvulsants, antineoplastic, or retinoid) are recognized as having an increased risk of developmental abnormalities when used clinically in humans [5]. However, since few drugs have been systematically studied to identify their full range of possible teratogenic risks, we cannot assume that current knowledge is complete. The identification of a drug's with teratogenic potential is important because drug- induced adverse foetus effects are potentially preventable.

Pattern of Medication use in Pregnancy

Pregnancy is a normal physiological change which may be accompanied by some common conditions which may occur normally due to the physiological changes for which drug treatment may be necessary. Thalidomide, prescribed for anxiety, insomnia and as an anti-emetic drug in pregnancy, turned out to cause phocomelia and other congenital anomalies in thousands of children exposed in uterus [13].

Hence to safeguard against such incidences, the regulatory authority such as Food and Drug Administration (FDA) has categorized use of drugs in pregnancy. Therefore it would be prudent for prescribers to prescribe drugs with caution in pregnancy. Studies have reported an increasing trend in drug use during pregnancy [14].

A Prospective study [18] reported that Iron, calcium and folic acid were the most frequently used drugs in pregnancy, accounting for 78.2%, 77.1% & 46.3% respectively. However, percentage encounter with antibiotic prescribed was 11.2%. Similarly, in a retrospective study in Finland, reported that 20.4% of women purchased at least one drug classified as potentially harmful during pregnancy and 3.4% purchased at least one drug classified as clearly harmful [15, 16] revealed in their surveyed carried out in Denmark that antibiotic was prescribed in 22.3% to pregnant women. A cross -sectional study conducted on pregnant patients in Benin city Nigeria revealed that folic acid was taken by 76,08% of all the pregnant women, while antimicrobial drugs were taken by 19.75%. About 15.83% used drugs with Doctors Prescription and 3.92% without a Doctor prescription [17].

Safe use of drugs in pregnancy is a responsibility of all members of the healthcare team and the consumers alike; nevertheless, the bulk of this responsibility rests on the Physicians shoulder. Drugs are responsible for up to 1% of reported cases of congenital malformations [18] therefore safety of drugs to the mother and her unborn baby has to be considered during drug prescribing. Drugs prescription in pregnancy and lactation would therefore require good knowledge of drug so as to prevent teratogenicity, foetus and neonatal effects that are associated with the drugs under consideration [19]. One year retrospective study conducted in teaching hospital Sokoto Nigeria revealed that anti-malarial were the most prescribe drugs 36.6%, but percentage encounter with antibiotic was found to be 43.6% [20]. Similar report was made in a retrospective study conducted in Benin City, Nigeria [21] that minerals and vitamins were the most 2396 (42.02%) frequently prescribed medicines in pregnancy, while antimalarials and antimicrobial were encountered at 640(11.2%) and 502(8.80%) respectively.

In developed countries there are systems in place to monitor pregnancies exposure to drugs and their outcomes. These data provide a population that can be compared with birth defect

prevalence in cohorts exposed to specific drugs [22]. In the United States, a prevalence of 1.5-2.5% major birth defects at birth has been reported [23, 24], a rate which includes heart defects, hip dysplasia and cleft palate. However, in resource-poor countries, population data on maternal outcomes and malformations are very limited [9].

Thus, nearly all developing countries rely on drug safety data from industrialised countries. However, there are no or limited safety data in pregnancy for drug targeting tropical diseases, as these are not widely use in the countries with more robust pharmacovigilance system [25]. Hence, determination of pattern of drug use in pregnancy and any additional risk associated with drug exposure during pregnancy in developing countries will be beneficial. This is the focus of this study. This study therefore set out to profile medication exposure during pregnancy, and assess neonatal risk following *in utero* drug exposure.

Methods

Study setting

The research work was conducted in Antenatal Care (ANC) clinics and obstetrics wards of six (6) healthcare facilities across all level of healthcare system in Edo State, Nigeria. The healthcare facilities were: General Hospital Afuze, Primary Healthcare Referral Centre Afuze, Otuo Health Centre, Ugbeku Health Centre Benin, University Benin Teaching Hospital (UBTH), and Central Hospital Benin, City. The study was performed between February, 2014 and May 2015.

Study Design

The study design was prospective observational study that enrolled pregnant women at their first antenatal visit to the health facilities and followed up till delivery.

Study Population/Recruitment Method

The population of interest was pregnant women, recruited at the Antenatal Care (ANCs) clinics of the study facilities. All eligible women were approached consecutively at the ANCs until a total of 2530 pregnant women were recruited into the study. Pregnant women, who visited ANC clinics in the study facilities, voluntary agreed to participate, agreed to be followed up to term and willing to give birth at the study facility was included in the study. However, those who refused to participate in the study; have a psychiatric or social condition that interferes with their ability to provide an accurate medical or drug history or give informed consent and reported that they will not give birth at the study facility were excluded.

Ethical Consideration

Ethical approval was sought and obtained from the Ethics Committees of University of Benin Teaching Hospital, and Edo State Health Management Board. In addition, administrative approvals were obtained from the hospital management of respective health facilities prior to the data collection process.

Data collection Instrument

Data collection forms were designed to capture relevant data. The form comprised two parts; the first collected demographic and obstetric information and second part was designed to capture information on medicals problems, medications (prescribed and none prescribed) being used, previous and current obstetric history.

Enrolment and Initial Assessment

A clinical talk was conducted at every study facilities in Pidgin English to the pregnant women on the safety of drug in pregnancy, healthy life style, the need to consult physician for any medical conditions, the purpose of the study, advantages of participation in the study and the rule guiding the study before the commencement of recruitment. Pregnant women, who came to Antenatal clinic (ANC) during current pregnancy and consented to participate in the study, were enrolled and had initial assessment. A case record form (CRF1) was used to documents demographic information, medical history, obstetric history, and drugs (prescribed and none prescribed) used, intermittent preventive treatments (IPT) and previous birth outcome. This information was obtained from women's ANC cards, medical case files and interviews. The form was used to establish whether the woman had exposure to any medicine during current pregnancy; if so, the timing of exposure and whether the exposure took place on the basis of a clinical or laboratory confirmed diagnosis. Various aids were introduced at the selected sites to improve women recall of drug exposures during pregnancy, this include tablets, treatment packages and visual identification chart. Figure 1 provides an overview of the procedures and assessments that were conducted in each of the facility during this study.

Second and Subsequent Antenatal Visits

At the end of each ANC visit, an appointment for the next ANC visit was made and contact details including telephone number of the women were taken and updated where necessary. Women were asked to return for follow-up assessments at normal scheduled ANC visits. The follow-up was generally divided into two to three contacts, depending on the gestational age of the enrolee. Follow-up were undertaken at gestational age of 12weeks, 27weeks, and above 36weeks. During the follow-up visits information such as obstetric and medical conditions, medications use (prescribed and self-administered), herbal medicines, smoking, and alcohol consumption were updated. At each ANC visit the women were counselled to return to the facility for delivery. This process was done for each enrolled pregnant women and followed- up till delivery.

Delivery and Neonatal Assessment

The labour wards staffs (Physicians, nurses, and other health care providers) identified enrolees by the attached form (CRF2) on the ANC cards. Immediately after delivery, the babies underwent a careful assessment for birth weight, head circumference, length and Apgar score as well as general physical examination. The detailed information gathered on pregnancy outcomes were recorded in the CRF2. Information on any spontaneous abortions or miscarriages, which terminate the pregnancy, was also recorded in this form. Other vital information recorded was neonatal sex, gestational age at birth, date of delivery, type of delivery (vaginal or caesarean section) and place of examination. All abnormalities observed

and adverse pregnancy outcomes in the babies were noted and reported in the CRF2.

Data Analysis

The data collected were entered into Microsoft Excel Spreadsheet and coded. These codes were transferred into the statistical package for Social Sciences (SPSS) version 20. Descriptive statistics was done and Drugs exposure profile was analyzed by "intention to treat" and "per protocol". These were compare by paired sample *t*-test method. A statistical signifiant level was set at p-value leess than 0.05.

Neonatal risk to the exposed drugs during pregnancy was assessed based on risk classification [26].

Results

Demographic and Obstetric Characteristics of the Enrolled Pregnant Women

In this study 2530 women were enrolled and 900 out of them were followed to delivery. About 95.5% of the enrolled women were age 21-35years, and a majority of them had secondary (46.4%, 2539) or tertiary education (47.4%, 1201). Most of the women were either business women (50%). Obstetric information obtained showed that majority of enrollees were multigravid (33.3%, 839), women of gestational age of (13-27) weeks post conception constituted (47.9%, 1126) while majority (70.6%, 1782) had history of vaginal live birth in their previous pregnancies (Table 1).

Profile of medical conditions treated

Table 2 shows the profile of medical conditions of the enrolled pregnant women in the six (6) health facilities. Malaria cases were most commonly encountered (51.9%, 2219), followed by Genito-urinary infections (36%). However only (1.2%, 5) of cardiovascular disease (hypertension) was encountered.

Profile of medications Prescribed during pregnancy

Table 3 and 4 shows the profile of prescribed drugs during pregnancy. About 6639 drugs were prescribed for the period under review. The distribution of six classes of medications, antimalarials, antimicrobials, analgesics, antihypertensive, antihistamine prescribed at the six health facilities is shown in Table 3. Antimalarials were the most frequently prescribed medications 889 (55.4%). Sulphadoxine/pyrimethamine (73.9%) 650 were the most frequently prescribed antimalarials drugs in the six health facilities. Other antimalarials prescribed include Artemether/Lumefantrin (24.9%) 221 and quinine (2%) 18. Antimicrobials agent constituted the second most commonly prescribed medications during pregnancy 316(19.7) .The antimicrobial prescribed were: antibacterial (68%) 215, antifungal (27.2 %,) 86 and antiretroviral agents (4.7%) 15. Other class of drugs encountered include antihypertensive 29(1.8%), antihistamine 23(1.4), and analgesics 56(3.5).

Drug exposure data of 2530 pregnant women enrolled (intention-to-treat) and 900 pregnant women followed up to delivery (per protocol) were collected to be 6630 and 2218 respectively. These were categorized based on anatomical therapeutic and chemical classification of pharmaceuticals, however, association between each classes of medications use in pregnancy of per protocol and intention- to- treat showed significant different in antihypertension and antihistamines while other classes showed no difference at $P > 0.05$ (Table 4). Most women self-medicated with analgesics (paracetamol) (90.2%) and Chloroquin (0.6%) (Table 5)

Profile of Medications prescribed at different trimesters of pregnancy

Almost all the medications used in this study, were prescribed most frequently at second and third trimesters. Out of (100%) 801 Antimalarials prescribed, (4.7%, 41), (66.7%, 588), and (28.6%, 252) were encountered in first, second, and third trimester respectively, however, (47.3%, 146) and (27.8%, 86) of antimicrobials were prescribed in second and third trimester respectively. Other classes of medications prescribed with high frequency in second and third trimester were antihypertensive, antihistamines, and analgesics. Antimicrobials drugs was the highest (24.9%, 77) prescribed drugs in first trimester while anticonvulsant and analgesics were the least prescribed. (Table 6).

Delivery and neonatal assessment at birth

About eighty six percent of women had vaginal delivery, 83.1% had term delivery, while 99.4% pregnancy outcome were live birth without any defects (Table 7). Table 8 shows that (14.4%) 97 had birth weight less than 2.5kg (underweight), about 92.6% and 98.7% had 7-10 Apgar score at 1minute and 5minutes, respectively. Physical examination shows that only 1 baby had extra digit. The high percentages of normal birth weight, Apgar scores child length signified that majority of children were born in sound health.

Table 9 shows that 47.5% (19) each of safe and low risk medications in pregnancy was prescribed to pregnant women during this study, while only 5% (5) of the high risk drugs was prescribed.

Table 1: Demographic and Obstetric characteristic of the enrolled pregnant women

Items	N (%)
Age(yrs)	
16-20	84(3.4)
21-35	2370(94.1)
>35	65(2.6)
Educational level	
Primary	137(5.4)
Secondary	1175(46.4)
Tertiary	1201(47.4)
Non formal	17(0.7)
Occupation	

Business	1267(50.3)
Civil servant	705(28.0)
Student	129(5.1)
Applicant	1(0.04)
Farmer	132(5.4)
House wife	276(11.0)
Clergy	7(0.3)
Gestational age at enrolment(wks)	
4-12	215(8.5)
13-27	1261(49.9)
28-40	1048(41.5)
Gravidity	
1	729(28.8)
2	896(35.4)
3	597(23.6)
4	292(11.5)
>4	15(0.6)
Previous pregnancy outcome	
Live birth	1782(70.6)
NA	720(28.5)
Miscarriage(1)	9(0.4)
miscarriage(2)	2(0.08)
Miscarriage(3)	2(0.08)
Still birth(1)	17(0.7)
Still birth(2)	2(0.08)
Still birth(4)	1(0.04)
Premature	1(0.04)
Hydrocephalic	1(0.04)

Key: NA= Not applicable, Wks=Weeks, Yrs=Years

Table 2: Profile of medical conditions among the pregnant women enrolled

Medical conditions	**N (%)**
Malaria	221(51.9)
Respiratory system	
Respiratory tract infections	23(5.4)
Genito-urinary system	
Urinary tract infections	13(3.1)
Pelvic inflammatory disease	10(2.4)
Candidiasis	22(5.2)
threaten abortion	1(0.2)
Gastrointestinal system	
Stomach cramp	27(6.4)
Constipation	23(5.4)
Heart burn	15(3.5)
Diarrhoea	2(0.5)
Peptic ulcer disease	4(0.9)
Typhoid	2(0.5)
Cardiovascular disease	
Hypertensive	5(1.2)
Skeletal muscle system	
leg cramp	2(0.5)
Pain	9(2.1)
Others	
Insomnia	38(8.9)
Human immunodeficiency syndrome	5(2.1)
Epileptic	1(0.2)

N = 421

Table 3: Classes of medications Prescribed during pregnancy

ATC category	**Drug type**	**N (%)**
J	Antimalarials	889(55.4)
J	Antimicrobials	316(19.7)

N	Analgesics	56(3.5)
C	Antihypertensive	29(1.8)
R	Antihistamine	23(1.4)
	Others	291(18.1)

N=1605

Keys: ATC= Anatomical therapeutic and chemical classification of pharmaceuticals. Other; (Vitamin s multivitamin)

Table 4: Medication prescribed for pregnancy 'per-protocol' and 'intention to treat'

ATC category	Drug type	Per protocol N (%)	Intention to treat N (%)	P- Values
J	Antimalarials			
	Artemether/Lumefantrin	58(13.3)	221(13.8)	
	Sulphadoxine/pyrimethamine	112(27.9)	650(40.4)	0.15
	Quinine	7(1.6)	18(1.1)	
J	Antibiotics			
	Amoxicillin	17(3.9)	100(6.2)	
	Co- amoxiclave	9(2.1)	40(2.5)	
	benzyl penicillin	5(1.1)	8(0.5)	
	Erythromycin	1(0.2)	12(0.7)	
	Azithromycin	5(1.1)	8(0.5)	0.0024
	Tinidazole	1(0.2)	27(1.7)	
	Metronidazole	5(1.1)	8(0.5)	
	Gentamycin	2(0.5)	3(0.2)	
	Cotrimoxazole	7(1.6)	9(0.6)	
J	Antifungal			
	Nystatin	2(0.5)	3(0.2)	
	Clotrimazole	1(0.2)	82(5.1)	0.0001
	Fluconazole	1(0.2)	1(0.06)	
J	Antiretroviral			
	Lamivudine	3(0.7)	5(0.3)	
	Zidovudine	3(0.7)	5(0.3)	1.0
	Nivirapine	3(0.7)	5(0.3)	
N	Analgesics			
	Paracetamol	17(3.9)	50(3.15)	
	Diclofenac	2(0.5)	2(0.1)	0.524
	Aspirin	1(0.2)	4(0.2))	
C	Antihypertensive			
	Methyldopa	8(1.8)	19(1.2)	
	Nifedifine	5(1.1)	9(0.6)	0.8
	Propranolol	1(0.2)	1(0.01)	
R	Antihistamine			
	Promethazine	1(0.2)	6(0.4)	
	Chlorpheniramine	5(1.1)	10(0.6)	0.2637
	Loratidine	7(1.6)	7(0.1)	
	Others	141(32.3)	291(18.1)	
	Total	436(100)	1605(100)	

Keys: ATC= Anatomical therapeutic and chemical classification of pharmaceuticals.

Table 5: Profile of self-medicated drugs in pregnancy followed-up to delivery

ATC category	Drug type	N (%)
J	Antimalarials	
	Chloroquin	1(0.6)
C	Analgesic	
	Paracetamol	156(90.2)
	Diclofenac	1(0.6)
B	Iron/multivitamins	
	Astyfer	3(1.7)
	Astymin	12(7.0)

Table 6: Medications prescribed at different trimesters of pregnancy

ATC Category	Drug type	1st trimester N (%)	2nd trimester N (%)	3rd trimester N (%)	Total N (%)
J	Antimalarials	41(4.7)	588(66.7)	252(28.6)	801(100)
J	Antimicrobial	77(24.9)	146(47.3)	86(27.8)	309(100)

N	Analgesics	1(1.7)	51(86.4)	7(11.9)	59(100)
C	Antihypertensive	3(11.5)	17(58.6)	9(25.9)	29(100)
A	Antidiarrhoeal	0(0)	3(75)	1(25)	4(100)
R	Antihistamines	2(9.1)	20(90.9)	0(0)	22(100)
N	Anticonulsion	1 (25)	3(75)	0	4 (100)

Keys: ATC= Anatomical therapeutic and chemical classification of pharmaceuticals.

Table 7: Delivery characteristics of 900 babies born by the enrolled women

Characteristic	N (%)
Mode of delivery	
Vaginal	772(85.8)
Cesarean sections	128(14.2)
Gestational age at birth (wks)	
<36	1(0.1)
37 – 40	748(83.1)
>40	151(16.8)
Neonatal Sex	
Male	506(56.2)
Female	394(33.8)
Pregnancy outcome	
Live birth	895(99.4)
Still birth	2(0.2)
Molar pregnancy expelled	2(0.2)
Spontaneous abortion	1(0.1)

N=900

Table 8: Neonatal assessment at birth

Assessment	N (%)
Birth weight (Kg)	
< 2.5	79(8.8)
2.6 – 4	597(66.3)
>4	224(24.9)
Neonatal examination	
Physically normal	899(100)
Malformation at birth	
Extra digit	1(100)
Head circumference(cm)	
.<32	1(3.7)
>33	26(96)
<50	6(17.6)
>50	28(82.4)
APGAR scores at 1min	
3-6.	41(7.4)
7-9.	514(92.6)
Apgar scores at 5min	
5-6.	7(1.3)
7-10.	543(98.7)

N=900

Table 9: Medications Prescribed during pregnancy and risk level

Safe In Pregnancy	Low Risk In Pregnancy	High Risk In Pregnancy
Amoxil	Bromazepam	Cotrimoxazole
Ascorbic Acid	Chloroquin	Propranolol
Ceftriaxone	Diazepam	
Chlorpheniramine	Diclofenac	
Cimetidine	Diphynoxylate	
Clotrimazole	Fluconazole	
Co-Amoxiclave	Gentamycin	
Erythromycin	Lamivudine	
Ferrous Sulphate	Loperamide	
Folic acid	Mebendazole	
Hyoscynamine	Nifedifine	

Magnesium Sulphate	Nivirapine	
Methyldopa	Omeprazole	
Metoclopramide	Pyrantrin	
Nystatin	Quinine	
Paracetamol	Sulphadoxine	
Promethazine	Tioconazole	
Simethicone	Tramadol	
Theophyllin	Zidovudine	

Safe in pregnancy (47%, 19/41), low risk (47&, 19/41) and high risk in pregnancy (5%, 2/41)

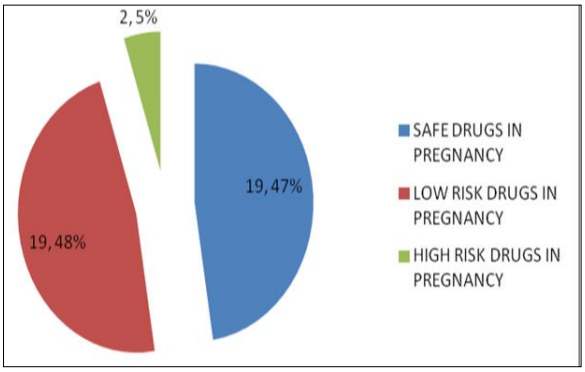

Fig 1: Risk assessment of drugs prescribed during pregnancy

Discussion

Majority of pregnant women enrolled were 20-35 years of age, which is similar to that obtained in study reported by WHO (2004) [27]. And represent normal reproductive age group. About half of the enrollees visited Antenatal clinic in second trimester which is similar to retrospective study conducted by Harsh *et al*, 2012 [18]. Most of women had normal life birth in their previous pregnancy outcome, while less than half visited ANC for the first time.

Malaria was the most prevalent medical conditions treated among enrolled pregnant women in the antenatal clinic of the six health facilities. Similar report was made by the previous study [21]. Malaria in pregnancy is known to be one of the common medical problems in Nigeria and other part of the world identified to as malaria endemic area. Malaria in pregnancy results in maternal anemia, intrauterine growth retardation, fetal low birth weight and neonatal mortality [28]. Genitor/urinary tract infections were the second most prevalence medical condition follows by gastrointestinal tract ailments. Others include insomnia, HIV and least treated medical condition was epilepsy. The pattern of distribution of these medical conditions informed the rate at which antimalarials and antimicrobials were used in this study. Antimalarial were the most frequently prescribed medication; however, Sulphadoxin/pyrimethamine was the most prescribed follow by artemether and Lumefantrin combination.This is Similar to what was obtained in some earlier studies [17, 21]. This observation could be due to the environmental poor control. However, prevention and treatment of malaria are important components of antenatal care in endemic area, but require adequate caution during pregnancy [21].

Antimicrobials were the second most frequently prescribed. Similar result was reported by Jimoh, 2011. Antibiotics are usually prescribed with caution due to the problem of drug resistance, bearing this in mind the higher percentage of antibiotics prescribed in the study could be due to high opportunistic infections, respiratory tract infections, urinary tract infection and pelvic inflammatory diseases (PID) which occur commonly among pregnant women.

Analgesic (paracetamol) and supplement (multivitamins) were the most frequent self-medicated drugs throughout the three stages of pregnancy this may be due to their availability, affordability, tolerability and lack of the known teratogenic effect of these drugs, this finding is similar to that obtained in some studies [19, 18]. This result could also be due to the fact that majority of the women were literate, thus, they may be adequately informed on the safe use of these drugs during pregnancy. Other drugs that were self-medicated include antimicrobials, antimalarials and anti-ulcer drugs. However, no record of smoking, and illicit drugs, but only one took alcohol. Most of the pregnant women were exposed to drugs during second trimester, follow by third trimester then first trimester. However, similar finding was reported[18]. This finding could mean that medicines were prescribed with caution by the prescribers at the study facilities. The finding could also be attributed to the fact that majority of the prescribers were trained physicians and this is encouraging.

The study revealed that majority of the birth outcome were normal live birth, however, few constitute unexpected outcomes such as preterm delivery, still birth, and spontaneous abortion, this result may be likely due to adverse effects of some drugs taken, disease conditions and other substances which the women encounter during pregnancy.

Neonatal Assessment revealed that few babies had foetus low birth weight. This could be due to malaria infection. Majority of APGAR score at 1minutes and 5minutes were within the normal range and only one child had an extra digit at metatarsal. The low incident of adverse pregnancy outcome encountered could be attributed to the fact that safe and low risk drugs constituted the majority of drugs prescribed for the period under review. Few adverse pregnancy outcomes were recorded, these include spontaneous abortion, preterm birth, still birth, and molar expelled. Those women were exposed to folic acid, Sulphadoxin/pyrimethamine, Cotrimoxazole, Iron, metronidazole, anti-toxoid, calcium and vitamin C. The observed adverse pregnancy outcome could be due to the risk associated with the classes of drugs used during pregnancy as mentioned, or may be due to medical, social and environmental factors which the women might have encounter with during pregnancy.

It is worth noting that all pregnant women exposed to herbs in first and second trimesters in addition to other classes of drugs who were followed to delivery did not present any form of foetus malformation, all had physically normal babies. This

result may be due to lack of teratogenic effect of the herbs and the drugs or the feotus were not adequately exposed to the substances, because foetus effects of substances depends on dose reaching the foetus, point in development when drug exposure occur, duration of exposure and susceptibility of the foetus.

The occurrence of high risk drugs in pregnancy was low. Rational drug use demand that such high risk drugs do not occur but the use of such drugs may be necessary in condition where benefit outweigh the risk [29]. In this study, majority of drugs prescribed were classified as safe and low risk in pregnancy. Similar results have been obtained in a previous study [21].

Conclusion

Antimalarial and antimicrobial were the most prescribed drugs among the pregnant women; others include antihypertensive, analgesics and antihistamines. Malaria was found to be the commonest medical condition treated during pregnancy, followed by respiratory tract infections. The occurrence of high risk drugs in pregnancy was considerable low, while safe and low risk drugs were mostly prescribed in the study. The study also revealed that majority of drugs was prescribed during 2nd and 3rd trimesters of pregnancy. Neonatal assessment shows that majority of babies were born physically normal (only one baby was observed to have congenital malformation - extra digit).

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