DRUG UTILIZATION IN PREGNANCY IN A SECONDARY HOSPITAL IN BENIN CITY, EDO STATE

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CERTIFICATION

This is to certify that this project work was carried out by Enehikhare Festus Uwagboe with matriculation number: **PHA1606773** in the department of clinical pharmacy and pharmacy practice, faculty of Pharmacy, university of Benin, Benin City, in partial fulfillment of the requirement for the award of my doctor of pharmacy (pharm D) degree.

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DEDICATION

I dedicate this work to my beloved parents and siblings whose prayers and support have not wavered over the years.

ACKNOWLEDGEMENT

All thanks to God almighty the creator and sustainer of my life, who has made this work possible

I extend my deep-seated appreciation to my supervisor, Pharm. AE Egonmwan for his kind corrections, and mentorship. I highly treasure the time spent working under your supervision.

Most importantly, I will always continue to appreciate my mother Mrs Enehikhare Rosemary for her financial support and parental upbringing which has guided me till date. Special appreciation to my loving sisters Enehikhare Imade, Enehikhare Ivie, Enehikhare Osaivbie, Enehikhare E.Adesuwa, and my brother Enehikhare Ernest,I LOVE YOU ALL.

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ABSTRACT

Background: Managing medical complications in pregnancy is a challenge to clinicians since only a few medicines have been specifically tested for safety.

Objectives: The prescription pattern for pregnant women who attended antenatal clinic visits was assessed and the level of adherence of prescribers to protocol on the use of medicines in pregnancy was assessed. The prevalence of different medical conditions among pregnant who attended the antenatal clinic was evaluated.

Methods: Medical case files of 201 pregnant women who attended antenatal clinic visits were systematically sampled and investigated from a population of 789 pregnant women who registered for antenatal clinic visits and received prescriptions within the period of study (December 2022 to May 2023). Disease pattern was determined from their diagnoses. The prescription pattern was assessed using WHO indicators, and the United States Food and Drug Administration classification of medicines according to risk to the foetus

Results: Among the 201 pregnant women, 56.72% were in the age group of 25-34, which happened to be the majority and represents the normal reproductive age. Among the medical conditions to which drugs were prescribed in different trimesters, malaria was the most common ailment which comprised 22.45%, 37.56%, and 29.53% in the first, second, and third trimesters respectively. Out of the total drugs prescribed, category A comprised 8.92%, category B 46.79% and category C 36.62%. Category D and X were not prescribed. The average number of drugs per prescription was 3.18, Percentages encountered with antibiotics, injections, and generics were 11.11%, 7.36%, and 86.70% respectively.

Conclusion: Malaria fever occurred most frequently (32.75%) followed by upper respiratory tract (11.91%) and fungal infection (8.68%) among the pregnant women. The average number of prescriptions per encounter was much higher than WHO standard, indicating occurrence of polypharmacy. There was no occurrence of contraindicated drugs. WHO core indicators of good prescription behaviour were adhered to with regard to the use of antibiotics, injections and generic names in prescriptions.

KEYWORDS: Pregnancy, teratogen, trimester, WHO coredrug

CHAPTER ONE

INTRODUCTION

1.1 BACKGROUND OF STUDY

Pregnancy is a period marked by significant physiological changes in a woman's body, posing unique challenges to clinicians managing medical conditions in expectant mothers (Cheney BE, 2002). The use of medications by pregnant women can carry potential risks of causing birth defects in the fetus. However, the recommendation to completely avoid all medications during early pregnancy is not practical and can even be risky (Banhidy F. et al, 2005).

Pregnancy introduces special considerations for drug treatment due to the possible teratogenic risks of certain drugs and the alterations in the mother's physiology in response to pregnancy. The physiological changes associated with pregnancy affect how medications are processed in the body (pharmacokinetics), and some drugs may cross the placenta, potentially harming the fetus (Banhidy F.et al, 2005). Concerns about medication use during pregnancy and breastfeeding have been influenced by historical events, such as the thalidomide crisis in the 1960s and the discovery of teratogenic effects associated with diethylstilbestrol in 1971 (Deborah E, et al, 2005). These incidents prompted the U.S. Food and Drug Administration (FDA) to establish stringent regulations regarding drug labeling and the use of medications during pregnancy, requiring evidence of safety and efficacy for any drug before it can be made available commercially (Ward RW, 2001).

In general, it is advisable to avoid drug treatment during pregnancy (Kazeem AO, et al, 2012). However, there are situations in which it becomes necessary because some patients were already receiving treatment for chronic conditions like diabetes mellitus, asthma, or hypertension before becoming pregnant. In such cases, careful selection of the most suitable drug for their condition is essential (Hansen WF, et al, 2002). Since pregnant subjects are typically excluded from animal studies and randomized clinical trials, our knowledge of the safety of most drugs during pregnancy mainly comes from post-market surveillance and data from regulatory agencies like the U.S. Food and Drug Administration (FDA) and the National Agency for Food and Drug Administration and Control (NAFDAC) in Nigeria.

In 1979, the U.S. Food and Drug Administration (FDA) introduced a system for assessing the pregnancy-related risks associated with pharmaceutical agents. This system classifies all drugs approved after 1983 into one of five pregnancy risk categories (A, B, C, D, and X). Type A is considered the safest, while type X is strictly contraindicated during pregnancy.

Furthermore, supplements like iron, folic acid, calcium, ascorbic acid, and vitamin B complex are often prescribed to meet the increased nutritional needs during pregnancy. Additionally, expectant mothers may be prescribed analgesics such as paracetamol, expectorants, antiemetics, antacids, and antibiotics for treating urinary tract infections (UTIs) (Briggs GC et al, 2005).

1.2 PHYSIOLOGICAL CHANGES IN PREGNANCY

Pregnancy begins with fertilization, the union of sperm and egg, which typically occurs in the woman's fallopian tubes. Following fertilization, the zygote, or fertilized egg, rapidly divides into a growing cluster of cells. Approximately 5 to 7 days after ovulation, the fertilized egg attaches to the uterine wall, initiating the formation of the placenta. The placenta plays a crucial

role in supporting the growing baby by facilitating the exchange of oxygen, carbon dioxide, amino acids, fats, vitamins, minerals, and waste products between the mother's bloodstream and the developing fetus. This phase, extending from implantation in the uterine wall until the eighth week, is referred to as the embryonic stage, marked by rapid development as specialized cells differentiate to form vital organs, the nervous system, skeletal structures, muscles, and blood. Following the eighth week, the developing baby is referred to as a fetus, measuring around 2.4 cm in length. At this stage, most internal organs are formed, and external features like eyes, nose, mouth, and ears begin to take shape (Moore PJ, 1994).

As the fetus and placenta grow, they impose increasing metabolic demands on the mother, leading to significant changes in her physiology and physical appearance. Weight gain is observed due to increased breast tissue, blood volume, and water, both intracellular and extracellular. The mother's stores are replenished with fat and protein accumulation. During a typical pregnancy, an average weight gain of 12.5 kg is noted, with about 1 kg attributed to increased protein. Notably, plasma albumin concentrations decrease, and fibrinogen concentrations increase. Total body fat content rises during pregnancy, and during the latter half of pregnancy, plasma lipids increase while triglycerides, cholesterol, and lipoproteins exhibit decreases immediately after childbirth. The LDL/HDL ratio rises during pregnancy (Moore PJ, 1994).

The impact of drugs on the developing fetus is contingent on the stage of fetal development and the drug's concentration and dosage (Porter RS, 2004). Limited information is available regarding the effects of drugs during conception and implantation. Women at risk of conceiving or planning to become pregnant should discontinue all nonessential medications 3 to 6 months before attempting conception (Sorensan MK. et al, 2004). During the embryonic period, drugs

taken early in pregnancy (between 15 to 21 days after fertilization) may either be ineffective, lead to fetal demise, or have no discernible effect. During this early stage, the fetus possesses a significant capacity to withstand birth defects. However, the period between the 3rd and 8th weeks after fertilization is especially sensitive to birth defects, as it corresponds to the period of organogenesis when major organs start to develop. Exposure to drugs during this time can result in miscarriage, apparent birth defects, or subtle yet long-term impairments that may manifest later in life (Porter RS, 2004). By the 9th week, the embryo is termed a fetus, and the focus shifts mainly to maturation and growth. While exposure to drugs during this period is not associated with severe birth defects, they may hinder the development and function of normally forming organs and tissues (Porter RS, 2004).

The effects of drugs are also influenced by the dose received by the fetus, which, in turn, depends on factors such as the mother's dosage, drug distribution in her bloodstream, placental function, the physiological and genetic condition of both the mother and fetus, as well as the extent of exposure to drugs, chemicals, or other environmental hazards (Yankowitz J. et al, 2001).

1.3 PHARMACOKINETICS IN PREGNANCY

The unique physiological changes associated with pregnancy have notable effects on the pharmacokinetics of drugs administered to pregnant women. Throughout pregnancy, several physiological alterations are observed. Plasma volume increases by 30-50%, along with corresponding increases in cardiac output and glomerular filtration rate, leading to reduced circulating concentrations of certain drugs, particularly those excreted renally. These changes can potentially decrease drug levels below therapeutic thresholds. Additionally, pregnancy induces an increase in body fat, which in turn augments the volume of distribution for fat-soluble

drugs. The reduction in plasma albumin concentrations during pregnancy leads to an expansion in the volume of distribution for highly protein-bound drugs, such as anticonvulsants. However, unbound drugs are eliminated more rapidly by the kidneys and liver, thereby counterbalancing the effect of expanded distribution. Furthermore, due to the influence of progesterone, gastric emptying time is significantly reduced in the third trimester, which may delay the onset of drug effects (Yankowitz J. et al, 2001).

The concurrent use of common medications during pregnancy, such as antacids, iron, and vitamins, has the potential to bind and deactivate certain drugs. When drugs are administered through intramuscular injection, they are absorbed more rapidly due to increased blood flow, which can enhance systemic drug absorption and the speed at which the drug takes effect (Yankowitz J. et al., 2001). Finally, estrogen and progesterone can modify the activity of liver enzymes, potentially resulting in drug accumulation or reduced drug excretion (Hansen W. et al., 2002).

1.4 PLACENTAL TRANSFER OF DRUGS

The placenta serves as the crucial link between fetal and maternal blood, creating a functional union. This remarkable organ performs various vital functions to ensure the well-being of both the developing fetus and the mother. These functions encompass providing nourishment, facilitating respiration, managing metabolism, aiding in waste elimination, and executing a range of endocrine activities. For a drug to exert either teratogenic or pharmacological effects on the fetus, it must traverse from the maternal circulation to the fetal circulation through the placenta, a process largely dependent on diffusion (Sorensan Mk. et al, 2004).

The rate at which drugs traverse the placental barrier hinges on their specific chemical characteristics. Factors such as protein binding capacity, pH, lipid solubility, and molecular weight profoundly influence this process (Kraemer K, 2002). It is essential to note that only the unbound, free form of a drug has the capability to traverse the placenta. During pregnancy, maternal plasma albumin levels decline while fetal albumin levels rise. Consequently, concentrations of free drug increase and are able to cross into the fetal circulation. Furthermore, fetal pH tends to be somewhat more acidic compared to maternal pH, making it more likely for weakly basic drugs to cross the placenta (Loebstein R. et al, 1997). Moderately lipid-soluble drugs can readily diffuse through the placental membrane, whereas drugs with a low molecular weight (below 1000 g/mol) cannot cross the placental barrier (Kraemer K, 2002).

During the third trimester of pregnancy, placental drug transport intensifies due to an upsurge in maternal and placental blood flow, a reduction in placental thickness, and an expansion of the placental surface area (Yankowitz J. et al, 2001).

1.5 PREGNANCY AND DRUG USE

Drugs play a crucial role in enhancing human health and promoting overall well-being. However, to achieve the desired therapeutic effects, drugs must adhere to the principles of safety, efficacy, and rational use (Sharma R. et al, 2006). In general, it is advisable to avoid drug usage during pregnancy whenever possible because drugs ingested by a pregnant woman can potentially reach the fetus, posing risks by crossing the placental barrier—a pathway shared with oxygen and nutrients necessary for fetal growth and development (Porter RS, 2004).

Despite the desirability of abstaining from medication during pregnancy, this isn't always feasible and can even be dangerous. Many women enter pregnancy with pre-existing medical

conditions that demand ongoing or intermittent treatment, such as asthma, epilepsy, or hypertension. Furthermore, new medical issues may arise during pregnancy, or existing ones may worsen, necessitating the use of pharmacological therapies. Failing to manage these conditions can have adverse effects on both the mother and the developing infant's health (Andrade SE. et al, 2004). Moreover, certain drugs like vitamins, minerals, iron supplements, and dietary enhancements are vital for the well-being of both the pregnant woman and the developing fetus. It has been reported that approximately 8% of pregnant women require drug treatment for various chronic diseases and pregnancy-related complications (Sharma R. et al, 2006). Additionally, many women take medications during the early weeks of pregnancy, often before they are aware of their pregnancy. Approximately 59% of pregnant women are prescribed medications other than vitamin or mineral supplements, and around 13% use herbal supplements (Andrade SE. et al, 2004). Moreover, over 90% of pregnant women, at some point during their pregnancy, use prescription medications, over-the-counter drugs, or substances with addictive properties such as tobacco, alcohol, or illicit drugs (Porter RS, 2004).

The reality that certain drugs utilized during pregnancy can harm the developing fetus presents one of the enduring dilemmas in medical practice (Yaffe SJ, 2002). Pregnant women are often excluded from clinical trials, and results from animal studies do not necessarily translate directly to human responses. Consequently, administering specific drugs to pregnant women poses considerable challenges, prompting most healthcare professionals to adopt a cautious approach to drug utilization during pregnancy. Concerns about fetal harm and even fatalities stemming from drug use during pregnancy have posed significant barriers to conducting clinical research on drug safety during this period. Consequently, information about the safety of drugs during pregnancy is primarily derived from case reports, epidemiological investigations, and animal

studies, all of which come with inherent limitations, making it challenging to accurately assess the risks associated with drug utilization during pregnancy (Ward RW, 2001).

A study conducted in 2001 revealed that there was an alarming lack of information regarding the risks and safety of over 90% of drugs approved by the FDA for use during pregnancy between 1980 and 2000 (Andrade SE. et al, 2004). This dearth of information poses a considerable challenge for both women and healthcare providers when it comes to deciding whether to use a particular drug during pregnancy.

Despite the limited knowledge available on the safety of medications during pregnancy, data on the usage of over-the-counter and prescription drugs indicate that the use of medications during pregnancy is widespread (Yaffe SJ , 2002). While it is true that roughly 2 to 3 percent of birth defects can be attributed to drug use, there are instances where medication is medically necessary to safeguard the health of both the expectant mother and her developing fetus. Healthcare professionals may recommend specific vitamin and mineral supplements for pregnant women to support their well-being during pregnancy (Porter RS, 2004). These medications are also commonly prescribed to alleviate various pregnancy-related symptoms, including body aches, nausea, vomiting, and edema (Pangle BL, 2006). Furthermore, medication may be administered to address conditions that arise during pregnancy but are unrelated to the pregnancy itself, such as upper respiratory tract infections, urinary tract infections, digestive disorders, and other non-pregnancy-related ailments. Pregnant women may also require medication to manage pre-existing chronic conditions like epilepsy, hypertension, or psychiatric disorders, or to address complications linked to pregnancy, such as gestational hypertension, premature labor induction, or the promotion of fetal lung maturation for preterm birth (Splinter MY.et al,1997).

Therefore, it is of utmost importance to assess the patterns of drug utilization during pregnancy in order to gain insights into how our current knowledge can be improved (De J LT. et al, 1990).

1.6 HOW DRUGS AFFECT THE FETUS

Medications consumed by pregnant women can impact the developing fetus through various mechanisms. These drugs may exert a direct influence on the fetus, potentially causing harm or interfering with normal development, which could lead to congenital abnormalities or fetal demise. They can also disrupt the functioning of the placenta, typically by narrowing blood vessels, thereby diminishing the supply of oxygen and essential nutrients to the fetus from the mother. This reduction in the flow of oxygen and nutrients can result in an underweight and underdeveloped baby. Additionally, these drugs can induce strong contractions of the uterine muscles, indirectly jeopardizing the fetus by restricting blood flow or provoking premature labor and delivery (Porter RS, 2004).

1.7 FDA CATEGORIES FOR DRUG USE IN PREGNANCY

In 1979, the Food and Drug Administration (FDA) established a classification system to assess the teratogenic risk of drugs, which takes into account the quality of data obtained from animal and human studies. This system offers valuable guidance for healthcare providers when making therapeutic decisions. Category A is considered the safest classification, but certain drugs falling under categories B, C, and D are also administered during pregnancy. Category X is the sole rating indicating that a drug is unequivocally contraindicated for use during pregnancy (Table 1). The table provided below (Table 2) lists some of the drugs commonly used during pregnancy, along with their respective FDA categorizations. It is crucial to highlight that some drugs have

been scientifically proven to be detrimental to the fetus, and their use during pregnancy should be avoided (Table 3) (Pangle BL, 2006).

TABLE: 1.1

FDA CATEGORIZATION OF DRUGS FOR USE IN PREGNANCY

Category	Description
A	Thorough and well-managed research involving pregnant women has not revealed an elevated likelihood of fetal abnormalities.
B	Animal research has not indicated any harm to the fetus. Nonetheless, there is a lack of sufficient and carefully conducted research involving pregnant women. Or Animal studies have demonstrated a negative impact, but comprehensive and well-conducted research in pregnant women has not been able to establish a risk to the fetus.
C	Animal experiments have indicated a negative impact, and there is an absence of adequate, well-conducted research involving pregnant women. Or There have been no animal studies, and there is a lack of comprehensive, well-controlled research involving pregnant women.

D	Research, whether it consists of well-conducted and comprehensive studies or observational studies, involving pregnant women, has revealed a potential risk to the fetus. Nonetheless, the advantages of the treatment may surpass the potential harm.
X	Research, including both rigorous, well-monitored studies and observational inquiries, conducted in animals or expectant mothers, has shown clear indications of fetal abnormalities. Consequently, the use of the product is strictly discouraged for women who are pregnant or may become pregnant.

FDA categorization of drugs for use in pregnancy (Pangle BL.2006).

TABLE: 1.2

COMMONLY USED DRUGS IN PREGNANCY AND THEIR CATEGORIES

Drugs	**Category**
Analgesics and Antipyretics	B and C
Acetaminophen	B
Phenacetin	B
Aspirin	C
Antiemetics	B and C
Doxylamine	B
Meclizine	B
Cyclizine	B
Dimenhydrinate	B
Antibiotics	B, C and D
Penicillin, Ampicillin, Amoxycillin,	B
Cloxacillin	B
Cephalosporins	B
Erythromycin	B
Gentamicin	C
Amikacin	C/D
Streptomycin	D
Sulphonamides	B/D
Tetracyclines	D
Amoebicides-	B
Metronidazole	
Anthelmentics	B

Piperazine	
Mebendazole	
Antimalarials	C
Antifungals	C
Anti TB Drugs	B and C
Ethambutol	B
INH(Isoniazid)	C
Rifampicin	C
Pyrazinamide	C
PAS(Para-aminosalicylic acid)	C
Vitamins	
B,C,D,E,folic acid	A
Hormones	
Thyroxin	A
Androgens	X
Estrogens	X
Progestogens-	
Dydrogesterone	B
Hydroxyprogestrone	D
Medroxyprogestrone	D
Norethindrone	X
Norgestrel	X
Bronchodilators	C

List of some of the commonly used drugs during pregnancy along with their categories as per FDA categorization(Nanavati MS,1994)

TABLE: 1.3

MEDICATIONS CONTRAINDICATED IN PREGNANCY

Drug	Comments
Vitamin A and its derivatives including isotretinein, accutane and etretinate	Significant risk of spontaneous abortion(Briggs G.G,2002) and risk of many significant anomalies (Lewes L. 2000).
ACE inhibitors	When utilized during the second and third trimester, this may result in fetal renal harm, a reduction in the volume of amniotic fluid, and abnormalities in facial features, limbs, and pulmonary structures (Porter RS, 2004).
Anticoagulants- warfarin	Utilization in the first trimester leads to issues such as underdeveloped nasal structures and a flattened nasal bridge, known as Fetal warfarin Syndrome. In the second and third trimesters, its usage is linked to a higher likelihood of fetal abnormalities (Sorensan Mk. et al, 2004).
- Heparin	Considered safe, but prolonged usage during pregnancy can lead to osteoporosis and a reduction in platelet count in expectant mothers (Porter RS, 2004).
Estrogen and Androgens	Genital tract malformations(Sorensan Mk.et al,2004).
Thyroid preparations-	
Methimazole	An overactive and enlarged thyroid gland.
Carbimazole	An overactive and enlarged thyroid gland.
Radioactive iodine	UnderactSorensenoid gland in fetus
Propylthiouracil	Safe (Porter RS,2004).

Anticonvulsants	
Carbamazepine	Risk of birth defects
Phenytoin, Phenobarbitone	A bleeding problem in the newborn that can be avoided if the pregnant woman consumes vitamin K orally daily for one month before giving birth or if the newborn receives a vitamin K injection shortly after delivery (Porter RS,2004).
	Risk of birth defects.
Trimethadione	Increased risk of miscarriage in the women
Sodium valproate	Elevated likelihood of fetal birth defects, which may encompass conditions like cleft palate and irregularities in the heart, facial features, skull, hands, or abdominal organs (Porter RS,2004).
Antidepressants- Lithium	Congenital anomalies, particularly affecting the heart, as well as symptoms like sluggishness, reduced muscle strength, diminished thyroid gland activity, and nephrogenic diabetes insipidus in the newborn. Ebstein's anomaly, a tricuspid valve malformation, has been observed in several fetuses exposed to this medication (Porter RS,2004).
NSAIDs	
Aspirin and other Salicylates	Prolonged onset of labor, early closure of the ductus arteriosus, neonatal jaundice, fetal brain injury, and bleeding issues in the pregnant woman during labor, as well as in the newborn after delivery. (Porter RS,2004).

Antibiotics- Tetracycline	Impaired bone development, permanent teeth discoloration (yellowing), and heightened vulnerability to tooth decay throughout the body. (Porter RS,2004).
Chloramphenicol	Gray Baby Syndrome (Porter RS,2004).
Ciprofloxacin	Possibility of joint abnormalities (seen in animals) (Porter RS,2004).
Kanamycin and Streptomycin	Injury to the fetus ear leading to hearing loss. (risk of ototoxicity) (Porter RS,2004).
Sulfonamides	Jaundice and brain damage in newborn (Porter RS,2004).
Antineoplastic agents-	
Busulfan	Congenital anomalies like inadequate prenatal growth, lower jaw underdevelopment, palate cleft, atypical skull bone development, spinal irregularities, ear malformations, and clubfoot. (PorterRS,2004).
Chlorambucil Cyclophosphamide Methotrexate	
Oral Hypoglycemic drugs	Low blood sugar levels in the newborn due to insufficient diabetes control in the pregnant woman. (Porter RS,2004).

List of some of the drugs whose use is contraindicated during pregnancy along with the harmful /damaging effects they may produce on the fetus

1.8 CONCERNS WITH OTC DRUGS

In India, due to the easy availability of drugs and limited access to healthcare services, a significant portion of drugs are used for self-medication to address common complaints and infections, rather than relying on prescribed medications. This practice exposes consumers to the

risks of adverse drug reactions and drug interactions (Sharma R. et al, 2006). While many over-the-counter (OTC) drugs can be safely used during pregnancy under the guidance of a physician, some are known to be unsafe. Product labels advise women who are pregnant, may be pregnant, or are nursing to consult a doctor before using OTC medications (Meadows M, 2001).

Aspirin is one such OTC drug that should be avoided during the final three months of pregnancy. In 1990, the FDA issued a warning emphasizing the importance of not using aspirin during the last trimester of pregnancy unless specifically instructed by a physician, as it may lead to issues in the unborn child or complications during childbirth. Over-the-counter non-steroidal anti-inflammatory drugs like ibuprofen also carry a similar warning regarding third-trimester use.

It's essential to highlight that limited knowledge exists regarding the effects of herbs and dietary supplements on fetal development, making it difficult to ascertain their safety for use during pregnancy. Therefore, it's not prudent to assume that a product is safe for pregnancy solely because it is available over-the-counter and labeled as natural (Meadows M, 2001).

1.9 OBJECTIVES OF STUDY

1.9.1 General objectives:

The present study aims to evaluate the pattern of drug utilization among pregnant women who attended antenatal clinic in St. Philomena Catholic Hospital, Benin city, Edo state, Nigeria.

1.9.2 Specific objectives

1. To investigate the disease pattern of pregnant women who attended the antenatal clinic.
2. To assess the prescription profile of pregnant women who attended the antenatal clinic.

3. To assess the level of adherence of prescriber to protocol on the use of medicines in pregnancy.
4. To assess the types and extent of prescribing of medicines according to risk to the foetus in Hospital.

1.10 JUSTIFICATION OF THE STUDY

There have been drug use studies in Nigeria.

Odusanya et al did a retrospective prescribing audit at primary health care facilities and reported an average of 7.27 and 4.99 numbers of medicines in Mushin and Ikeja Lagos Nigeria, respectively.

Gharoro and Igbafe showed that out of the 1200 pregnant women in their study, self-medication occurred in 26.8%. Folic acid was used by 76.08% of the women, antimalarials 19.45%, however studies on prescribing in pregnancy are quite few in Nigeria, hence this study is done to add to the baseline of research of this sort.

CHAPTER TWO

METHODS

2.1 STUDY DESIGN

This was a Six months retrospective study (December 2022 to May 2023). The study was conducted on pregnant women who registered for Antenatal Clinic (ANC) and received prescriptions in a Secondary Hospital in Benin city,Edo State, Nigeria (St. Philomena Catholic Hospital). .

2.2 STUDY LOCATION

The research was carried out at St. Philomena Catholic Hospital, a healthcare facility situated in Benin City, Edo state. This hospital offers a wide range of medical services, including general medical care, Gynaecology and Obstetrics treatments, internal medicine, surgery, Ophthalmology, Dermatology, and Physiotherapy.

2.3 STUDY POPULATION

During the specified study period, 789 pregnant pregnant women of the 869 pregnant women that registered for ANC visit were eligible for the study.

2.4 INCLUSION CRITERIA

- Pregnant women from 16 years and above.
- Pregnant women that received prescriptions during antenatal clinic visits.

2.5 EXCLUSION CRITERIA

- Pregnant women with confusing medical information.
- Illegible prescriptions

2.6 SAMPLE SIZE DETERMINATION

The study population was obtained from the antenatal clinic records of the Hospital.

The sample size for the study was calculated using the Yamane formula,1967, for sample size determination.

$n_o = \frac{N}{N(e^2)+1}$

n_o= sample size

N= population size (789)

e= margin of error (5%)

$n_o = \frac{789}{789(0.05^2)+1} = 265$

However, 204 medical case files were utilized for the study.

A systematic Sampling technique (every odd number) was used for selecting representative samples from the population.

1.7 DATA COLLECTION

The necessary data, including patient age, place of residence, gravidity, prescribed medications, dosage form, administration route, primary diagnosis, the trimester of drug use, and other

relevant details, were gathered from the patients' records using a well-structured data collection form.

This data collection form was divided into four sections. Section A was designed to capture the patients' demographic information, while Section B focused on their obstetric details. Section C pertained to the medical conditions of pregnant women from their initial ANC (Antenatal Care) visit to delivery. Section D centered on pregnancy outcomes. The questionnaire items in the data collection form were adapted from previous studies such as those conducted by Fikadu M et al. in 2015, Kosisochi C A et al. in 2019, and Eze UI et al. in 2007.

Data collection commenced on June 1, 2023, and concluded on July 12, 2023.

1.8 DATA ANALYSIS

The collected data was inputted into a spreadsheet and subjected to analysis using descriptive statistics. Subsequently, the statistical software package commonly used by social science researchers, SPSS version 17.0, was employed for further analysis. The core prescribing indicators, as outlined by WHO/INRUD, were utilized in this analysis.

To determine the average number of medications per patient encounter, we divided the total count of drugs by the number of patient encounters. The percentages of encounters involving generic names, antibiotics, and injections were calculated by dividing the total occurrences of each by the overall number of encounters and then multiplying by 100.

CHAPTER THREE

RESULTS PRESENTATION

TABLE3. 1: DEMOGRAPHIC CHARACTERISTICS OF PREGNANT WOMEN

Characteristics	Frequency	Percentage
AGE		
18-24	34	16.92
25-34	114	56.72
35-44	49	24.38
≥45	3	1.49
Missing	1	0.5
EDUCATION		
None	1	0.50
Primary	2	1.00
Secondary	66	32.84
Tertiary	132	65.67
MARITAL STATUS		
Single	4	1.99
Married	194	96.52
Widow	0	0.00
Divorced	0	0.00
Missing	3	1.49
OCCUPATION		
Civil Servant	39	19.40

Self-employed/Trader	143	71.14
Full time house wife	7	3.48
Student	10	4.98
Missing	2	1.00
RESIDENT		
Rural	2	1.00
Urban	198	98.51
Missing	1	0.50
RELIGION		
Christian	191	95.02
Muslim	4	1.99
Missing	6	2.99

A total of 201 pregnant women medical records were utilized for the study.

Among the 201 pregnant women, 34(16.92%) were in the age group of 18-24years, 49(24.38) were in the age group of 35-44,the ages of 3(1.49%) were greater than 45, the age of 1(0.5) was not stated, while 114(56.72%) were in the age group of 25-34, which happened to be majority and represents the normal reproductive age. Among the pregnant women,1(0.5) had no formal education, 2(10) had primary education,66(32.84) had secondary education, while majority of them ,132(65.67) had tertiary education as their highest level of education.

With regard to their marital status,4(1.99) were single, majority of the pregnant women,194(96.52) were married, while the marital status of 3(1.49) was not stated

TABLE3.2:OBSTETRIC CHARACTERISTICS OF PREGNANT WOMEN WHO WERE ATTENDING ANC

PARAMETER	FREQUENCY	PERCENTAGE
Gravidae		
Primigravida	50	24.88
Secundum gravida	49	24.38
Multigravida	93	46.27
Gravidae not indicated	9	4.48
Time of first ANC visit		
First trimester	72	35.82
Second trimester	115	57.21
Third trimester	14	6.97

Among the total pregnant women, 24.88%(50) were primigravidae, 49(24.38) were secundum gravidae while the majority (46.27%) were multigravidae, but for 4.48% of them gravidity was not stated.

TABLE 3.3: PREGNANCY OUTCOME

	Frequency	Percentage (%)
Live birth		
Normal baby	195	97.01
Abnormal	0	0
Death(Still birth)	5	2.49
Missing	1	
Pregnancy termination	0	0
No pregnancy termination	197	98.01
Missing	4	1.99
APGAR Score		
0 to 3	1	0.50
4 to 6	0	0.00
7 to 10	195	97.01
Missing	5	2.49
Birth Weight		
Less than 2.5kg	16	7.96
2.5kg to 4kg	169	84.08

Greater than 4kg	7	3.68
Missing	9	4.48

Pregnancy outcome showed that 195(97.01%) of the women had live births with no deformities while 5 of them had still births. Majority of the babies had normal APGAR SCORE of seven and above for both 1 and 5minutes after birth. Of the 201 babies,16(7.96%) had low birth ,7(3.68%) had fetal macrosomia and majority,169(84.08) had normal birth weight (2.5kg to 4kg) as presented in table 3.

TABLE 3.4:FREQUENCY DISTRIBUTION OF MEDICAL CONDITIONS AMONG THE PREGNANT WOMEN

	Frequency (%)		
Diagnosis	**1st trimester**	**2nd trimester**	**3rd trimester**
Prophylaxis	7(14.29)	22(10.73)	10(6.71)
Malaria	11(22.45)	77(37.56)	44(29.53)
URTI	1(2.04)	26(12.68)	21(14.10)
Pains	5(10.20)	10(4.87)	6(4.02)
High BP	2(4.08)	13(6.34)	18(12.08)
Fungal infection	5(10.20)	15(7.32)	15(10.07)
Nausea and vomiting	4(8.16)	2(0.98)	0(0.00)
UTI	0(0.00)	1(0.49)	3(2.01)
PUD	6(12.24%)	14(6.82)	6(4.02)
Itching	2(4.08)	5(2.44)	1(0.67)
GIT infection/Diarrhea	0(0.00)	3(1.46)	4(2.68)
Premature contraction	0(0.00)	4(1.95)	7(4.50)
Conjunctivitis	0(0.00)	0(0.00)	1(0.67)
Other infections	1(2.04)	0(0.00)	2(1.34)
Anemia	1(2.04)	3(1.46)	0(0.00)
Sepsis	0(0.00)	6(2.94)	6(4.02)
Other medical conditions	4(8.16)	4(1.95)	5(3.36)
TOTAL:	49(100)	205(100)	149(100)

Among medical conditions to which drugs were prescribed in different trimesters, malaria was the most common ailment which comprises 22.45%, 37.56%, and 29.53% in first, second and

third trimester respectively.Upper respiratory tract infection was more in second and third trimester(12.68% and 14.10% respectively).Fungal infection was also commonly reported in all the trimesters while Nausea and vomiting was more frequent in first trimester. Urinary tract infection(UTI), diarrhea, anemia, conjunctivitis were the least frequent as shown in Table4.

TABLE3.5: DISTRIBUTION OF DOSAGE FORMS PRESCRIBED TO PREGNANT WOMEN WHO ATTENDED ANC FOLLOW UP

	Frequency (%)			
Dosage form	**1st trimester**	**2nd trimester**	**3rd trimester**	**Total**
Tablets	51(79.69)	247 (76.23)	19 (77.82)	491
Capsule	0 (0.00)	7 (2.16)	5 (2.02)	12
Syrup	7 (10.94)	30 (9.26)	16 (6.45)	53
Vaginal cream	5 (7.81)	15 (4.63)	13 (5.24)	33
Injectable solution	1 (1.56)	25 (7.72)	19 (7.66)	45
Eye ointment/eye drop	0 (0.00)	0 (0.00)	1 (0.40)	1
Topical cream	0 (0.00)	0 (0.00)	1 (0.40)	1
Total	64 (100)	324(100)	248 (100)	636

From the total dosage forms prescribed to the pregnant women, more than half of them (77.82%) were in tablet dosage form. It was the most commonly prescribed dosage form across all trimesters. Others like injectable solution, vaginal cream and syrup were also frequently prescribed (Table 5).

TABLE3. 6: ROUTE OF ADMINISTRATION OF PRESCRIBED DRUGS FOR PREGNANT WOMEN ATTENDING ANC

	Frequency (%)		
Route of administration	**1st trimester**	**2nd trimester**	**3rd trimester**
Oral	59 (90.77)	287 (88.04)	209 (84.27)
IM	1 (1.54)	12 (3.68)	12 (4.84)
Vaginal	5 (7.69)	13 (5.24)	13 (5.24)
Topical	(0.00)	1 (0.31)	4 (1.61)
IV	0 (0.00)	13 (3.99)	10 (4.03)

IM=intramuscular, IV= intravenous

Dosage forms such as tablets, capsules and syrup were administered orally while injectable solutions were prescribed to be administered via intravenous and intramuscular route.

TABLE3.7: FDA CATEGORY OF DRUGS PRESCRIBED TO PREGNANT WOMEN

	Frequency (%)			
FDA CATEGORY	**1st trimester**	**2nd trimester**	**3rd trimester**	**Total**
A	9 (13.85)	33 (10.15)	15 (6.02)	57 (8.92)
B	35 (53.85)	147 (45.23)	117 (46.99)	299(46.79
C	19 (29.23)	115 (35.38)	100 (40.16)	234(36.62)
D	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)
X	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)
NC	2 (3.08)	30 (9.23)	17 (6.83)	49 (7.)

NC=NON-FDA CATEGORISED

From the total drugs prescribed for the pregnant women, FDA category B drugs(46.76%) were the most commonly prescribed drugs followed by category C and A which account for 36.62% and 8.92% respectively.FDA category C and D were not prescribed, however, 7.67% of the total drugs prescribed were not FDA categorized.

TABLE3.8: FDA CATEGORY OF DRUG PRESCRIBED TO PREGNANT WOMEN

FDA Drug Category	**Frequency (%)**	**Representative drug**
A	57(8.92)	Ferrous sulphate, Folic acid, multivitamins, pyridoxine,

		Vitamin B complex, Vitamin C
B	299(46.74)	Metoclopramide, Amoxicillin, Amoxicillin/ clavulanic acid, metronidazole, Methyldopa, Tinidazole, Cloramphenicol eye ointment, Paracetamol, dydrogesterone, azithromycin, Loratidine, loperamide.
C	234(36.62)	Antacid syrup, Omeprazole, Nifedipine, Tramadol, Pentazocine, calcium gluconate, Artesunate, Artemeter/ Lumefantrine, Sulphadoxine and pyrimethamine, Alpha beta arteether, Salbutanol, hydaloxine.
D	0(0.00)	Not prescribed
X	0(0.00)	Not prescribed
Non FDA Category	49(9.67)	Maintenance fluids, combined cough syrup

All the FDA category A drugs prescribed for patients were minerals and vitamins; namely, ferrous sulphate, folic acid, multivitamin, vitamin B complex and pyridoxine. The majority of category B drugs prescribed for pregnant women were antibiotics such as amoxicillin, amoxicillin/clavulinic acid, metronidazole, tinidazole, and chloramphenicol eye ointment. Antihypentensive drugs such as methydopa and paracetamol (analgesic) were also among the most prescribed FDA category B drugs. Nifedipine, clotrimazole, pentazocine ,promethazine and the antimalarials such artesunate and artemether/lumefantrine were the most frequently prescribed FDA category C drugs. Maintenance fluids and combined cough syrup were the Non-FDA categorized drugs prescribed.

TABLE3. 9: PRESCRIBING PATTERN INDICATORS

	Value n (%)				
Indicators	**1st trimester**	**2nd trimester**	**3rd trimester**	**Total**	**Reference**
Average number of drugs per prescription	65/72 (0.90)	325/115 (2.83)	249/14 (17.79)	639/201 (3.18)	1.6-1.8
Percentage of encounters with antibiotics prescribed	0/65 (0.00%)	35/325 (10.77%)	36/249 (14.46%)	71/639 (11.11%)	20-26.8
Percentage of encounters with injection prescribed	1/65 (1.54%)	27/325 (8.31%)	19/249 (7.63%)	47/639 (7.36%)	13.4-24.1
Percentage of drugs prescribed by generic name	57/65 (87.69%)	287/325 (88.31%)	210/249 (84.34%)	554/639 (86.70%)	100

Majority of the drugs (86.70%) were prescribed by their generic names which was almost the same across all trimesters. Average numbers of drugs per prescription was 3.18, but this figure was relatively lower in first trimester (0.90). Percentages of encounters with antibiotics were 0.00%, 10.77%, 14.46% in first, second and third trimesters, respectively. The percentage of prescriptions with an injection prescribed was 7.36%. Most of injections containing prescriptions were prescribed in third trimester and second trimester(table 9).

CHAPTER 4

DISCUSSION

The results of this study revealed that the various medical conditions during pregnancy warranted the use of different types of drugs.

The majority of the women (56.72%) were of reproductive age (25-34), and virtually all (96.52%) were married, most likely due to socio-cultural and religious views, as observed by (Kosisochi CA et al, 2019). Indigenes in South-South Nigeria are mostly Christians, and having children out of wedlock is frowned upon (Sampson IT,2011). According to earlier studies (Kosisochi et al, 2019; Abubakar KI, et al, 2014), the majority of the patients (65.67%) had completed tertiary education. In addition, 71.14% of the women were self-employed. Because of the ease of access, nearly all of the ladies who visited lived in the urban community (98.51%).

Antenatal clinics were mainly visited by women in their first (35.82%) and second (57.21%) trimesters. This is consistent with the results of research conducted in India (Dereje Kebebe et al, 2015). However, another study conducted at a tertiary care hospital in Nigeria, Ebonyi, found that the majority of pregnant women sought antenatal care during the second and third trimesters (Kosisochi CA et al , 2019). Maternal factors such as health status during current pregnancy, unknown appropriate time for hospitalization, exposure; sociocultural factors such as preference for mothers-in-law, friends or advice from other women during the first weeks of pregnancy; religious factors such as preferences for prayer and faith healing; Institutional factors such as long waiting times and frequent antenatal care follow-up times cause pregnant women to schedule antenatal care appointments late (Nwaneri AC, et al, 2018).

Women with multiple pregnancies (multigravid) accounted for the majority (46.27%) in this study. This corroborates the findings of studies conducted in Sokoto and Edo States, both in Nigeria (Abubakar KI et al., 2014 and Eze UI, et al. 2007). Nigerian families seem to have an advantage in having more than one child. Although 99% of all maternal deaths occur in developing countries, the global maternal mortality rate has decreased by approximately 44% between 1990 and 2015 (WHO, 2019). Despite the fact that late booking of antenatal care is common among pregnant women in Nigeria, women with multiple pregnancies are more experienced than first-time pregnant women as they may have visited antenatal clinics during their previous pregnancy (Nwaneri AC, 2018).

Malaria (32.75%), upper respiratory tract infections (11.91%), and fungal infections (8.68%) were the most common medical conditions. In a similar study conducted in Benin-City, Edo State, Nigeria, malaria was the most common disease (38.3%), followed by upper respiratory tract infections (12.8%) and gastrointestinal infections (11.6%) (Eze UI et al, 2007). . Malaria is the most common medical condition among the three in all quarters. Malaria during pregnancy is a major public health problem in Nigeria as well as other malaria-endemic countries (WHO, 2004). Malaria during pregnancy causes anemia in the mother, intrauterine growth retardation, low birth weight of the fetus and neonatal death (WHO, 2004).

Hence, the majority of the medications prescribed were drugs used for the above medical conditions such as artemeter/lumefantrine, artesunate, amoxicillin, clavulanic acid, metronidazole, paracetamol, tramadol, pentazocine, omeprazole, gestid, rulox, among others. All of the drugs were either from FDA category A,B or C.

Oral dosage form was the main(84.27%) dosage form used across all trimesters as it is the simplest and easiest way for any patient to take a medication .This is in accordance with similar study performed in India (Dereje et al, 2015). Injectable products were used more in second and third trimester than in first trimester .

There were no occurrences of contraindicated medicines in all the trimester. Proper prescribing demands that contraindications do not occur but the use of contraindicated medicines may be considered in cases where benefits outweigh the risk (Beyens MN et al,2003). Majority of the drugs prescribed were in category B(46.79%) of the FDA's classification of medicines according to risk to the foetus, followed by those in category C(36.62%) and A(8.92%) respectively. No category D and X drugs were prescribed, however, 7.67% of the total prescriptions were not categorized. Similar study reported category A as the majorly prescribed drug, however, category D prescriptions were reported with no category X prescriptions (Eze UI, et al, 2007).

The average number of drugs per prescription was below the WHO range in the first quarter, but above the range in the second and third quarters, with a median value of 3.18. Similar results were obtained in Sokoto where the average number of drugs per prescription was 3.1 and in Benin City it was 3.0 (Abubakar KI et al, 2014, Eze UI, 2007). During pregnancy, there may be comorbid conditions that require the prescription of multiple medications in conjunction with the use of conventional medications such as iron preparations, folic acid, ascorbic acid and vitamin complex tablets. B (Abubakar KI et al 2014). Rational prescribing involves maximizing clinical and financial efficiency, minimizing harm while respecting patient choice (Onder G et al. 2017. Polypharmacy Differences occur when a person takes many different medications at the same time, which can increase the risk of drug interactions, side effects, poor treatment compliance,

and increased costs. Possible causes of polypharmacy include poor knowledge of appropriate prescribing, lack of evidence-based guidelines, and prescriber incentives.

The percentage (11.11%) of encounters with an antibiotic prescribed was lower than the WHO reference value which is commendable, consistent with result obtained in another study (Eze UI, et al 2007). Antibiotics should only be prescribed when there is justification for use. Irrational prescribing of antibiotics is associated with the development of resistance.

Percentage of drugs prescribed by generic name was almost the same across all trimesters, and the majority(86.70%) of them were prescribed by their generic name which is encouraging. Similar finding was reported in India (Dereje K et al, 2015).

Among the pregnant women, 97.01% gave birth to live babies with no deformities and APGAR SCORE within the range of 7 to 10 for both 1 minute and 5 minutes.This could be attributed to the fact that no contraindicated medicines were prescribed. Still birth was however recorded in 5 pregnant women.

Pregnancy induced hypertension (PIH) was the major cause of low birth weight (7.96%).

CHAPTER 5

CONCLUSION

Malaria fever occurred most frequently followed by upper respiratory tract infections and fungal infection among the pregnant women. The average number of prescriptions per encounter was much higher than the WHO standard, indicating an occurrence of polypharmacy, however this was lower in first trimester.

There was no occurrence of contraindicated drugs as all the medical conditions were managed with FDA category A, B and C drugs. WHO core indicators of good prescription behaviour were adhered to with regard to the use of antibiotics, injections and generic names in prescriptions.

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