ABSTRACT
Managing medical complications in pregnancy is a challenge to clinicians.
Objectives: This study profiled some disease and prescription patterns for pregnant women attending antenatal clinics (ANCs) in Nigeria. A risk classification of the medicines was also determined.
Methods: Medical case files of 1,200 pregnant women attending antenatal clinics of 3 health facilities in Benin City, Nigeria were investigated. 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: A total of 1,897 prescriptions of the 1,200 pregnant women attendees during the period under review were evaluated. Results indicated that malaria 554 (38%) was the most prevalent disease, followed by upper respiratory tract infections (URTIs, 13%) and gastrointestinal disturbances (GIT, 12%). The average number of drugs prescribed per encounter was found to be 3.0, and 2,434 (43%) of medicines were prescribed by generic name. Minerals/ Vitamins 2,396 (42%) were the most frequently prescribed medicines, and antibiotics occurred in 502 (8.8%) of the total medicines. Of all medicines prescribed, 984 (17%) were included in the foetal risk category C and 286 (5%) in category D.
Conclusion: The study concluded that malaria fever occurred most frequently followed by URTIs and GIT disturbances among the pregnant women. Minerals, vitamins and to a less extent anti-malarials topped the list of the prescribed medicines. The average number of medicines per encounter was much higher than WHO standards. The occurrence of contraindicated medicines was low.
Keywords: Teratogens. Pregnancy. Maternal Exposure. Nigeria.

INTRODUCTION
Pregnancy is a time of profound physiological changes in a woman’s body. These unique changes challenge clinicians managing disease states during pregnancy in the selection of medications best suited to treat their patients. Maternal drug use during pregnancy may pose a teratogenic risk to the foetus.
foetus. However, the recommendation to avoid all drugs during early pregnancy is unrealistic and may be dangerous.\textsuperscript{2,3} Pregnancy should not deter clinicians from providing their patients with appropriate management of their medical conditions, hence, prescribing in pregnancy is an unusual risk benefit situation.\textsuperscript{4,5}

In 1979, the United States Food and Drug Administration (FDA) introduced a system of rating pregnancy-risk associated with pharmacological agents. This system categorised all drugs approved after 1983 into one of five pregnancy risk categories (A, B, C, D, and X). It indicates the effect of the agent on the foetus based on available animal and human data and recommends the degree of precaution that should be undertaken with each drug. However, the risk factors assigned are sometimes difficult to interpret because they may not always reflect the latest findings.\textsuperscript{5}

Information on the use of drugs during pregnancy is scarce and rather anecdotal.\textsuperscript{6} Despite the absence of adequate studies on the safety and effectiveness of prescription drugs for pregnant women, evidence available shows that physicians prescribe, and pregnant women take a surprisingly large number of drugs. An international investigation sponsored by WHO showed that pregnant women ingest an average of three prescription medications during pregnancy (range 1 – 15). Furthermore, 86% of the women had taken at least one prescription medication during their pregnancies.\textsuperscript{5}

There have been drug use studies in Nigeria. Odusanya et al.\textsuperscript{9} did a retrospective prescribing audit at primary health care facilities and reported an average of 7.27 and 4.99 number of medicines in Mushin and Ikeja Lagos Nigeria, respectively. Gharoro and Igbafe\textsuperscript{10} 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 who had taken at least one prescription medication during their pregnancies.\textsuperscript{5}

Other medical conditions. 74 (5.2)

Table 1: Profile of medical conditions among the pregnant women

| Medical condition               | Frequency (%) |
|---------------------------------|---------------|
| Malaria fever                   | 554 (38.3)    |
| Upper respiratory tract infection| 185 (12.8)    |
| Gastrointestinal infection      | 167 (11.6)    |
| Urinary tract infection         | 154 (10.7)    |
| Pains                           | 110 (7.6)     |
| Other infections                | 37 (2.6)      |
| Premature contractions          | 30 (2.1)      |
| High Blood Pressure             | 28 (1.9)      |
| Nausea / Vomiting               | 24 (1.7)      |
| Insomnia                        | 21 (1.5)      |
| Numbness of fingers             | 16 (1.1)      |
| Itching                         | 14 (1.0)      |
| Co-morbid conditions            | 13 (0.9)      |
| Mastitis                        | 12 (0.8)      |
| Edema                           | 6 (0.4)       |
| Other medical conditions.       | 74 (5.2)      |
| Total                           | 1445 (100)    |

A total of 1897 prescriptions were obtained from the 1200 medical case files. The average number of drugs per encounter was found to be 3.0 (range 1 – 10). Eighty-two different medicines were encountered and a total of 5708 medicines were prescribed for the entire period. Table 2 shows the WHO prescribing indicators that were evaluated.
The distribution of medicines prescribed to these pregnant women is as shown in Table 3. Minerals and vitamins were the most frequently prescribed medicines. Folic acid 671 (35.4%) was the most frequently prescribed drug in the three health facilities. Other minerals and vitamins prescribed included ferrous sulphate 645 (34%), vitamin C 152 (8.0%) and calcium lactate 19 (1.0%). Paracetamol 749 (87.9%) was the most frequently prescribed analgesic; other analgesics included methamizole 66 (7.8%), acetylsalicylic acid 27 (3.2%), piroxicam 4 (0.5%), pentazocin 2 (0.3%), dihydrocodeine 2 (0.3%), and ibuprofen 2 (0.3%).

Antimalarials were the third most occurring medicines with an average of 640 (11.2%) for the three health facilities when compared with other groups of medicines. Chloroquine 350 (54.7%) was the most frequently prescribed antimalarial drugs for the 3 health facilities. Other antimalarial written included sulphadoxine/pyrimethamine 130 (20.3%), pyrimethamine 64 (10%), quinine 76 (11.9%), amodiaquine 48 (7.5%), proguanil 4 (0.6%), sulphamethopyrazine/pyrimethamine 2 (0.3%). Twenty different types of antibiotics were encountered in the study. Penicillins 279 (55.6%) were the most frequently used antibiotics for the antenatal clinics. Other antibacterial agents included metronidazole 59 (11.8%), macrolides 53 (10.6%), cotrimoxazole 37 (7.4%), phythalysulphathiazole 27 (5.4%) 4-quinolones 12 (2.4%), nitrofurantion 12 (2.4%), aminoglycosides (91.8%), and tetracycline 1 (0.2%).

A classification of medicines according to risk to the foetus indicated that of all the medicines prescribed, 2743 (48.1%) were in category A, 1465 (25.7%) category B, 984 (17.2%) category C and 286 (5.0%) in category D. Table 4 shows drugs and their frequency of occurrence in this study.

Table 2: Prescribing indicators encountered

| Prescribing Indicator | Value obtained | Reference value |
|-----------------------|----------------|-----------------|
| Average number of medicines per encounter | 3 (range 1 – 10) | 1.6 – 1.8 |
| Percentage of medicines prescribed by generic name | 42.7 | 100 |
| Percentage encounter with injectables | 5.8 | 13.4 – 24.1 |
| Percentage encounter with antibiotics | 8.8 | 20 – 26.8 |

Table 3: Frequency distribution of the medicines prescribed

| Prescribed Medicines | Total (%) |
|----------------------|-----------|
| Minerals /Vitamins   | 2396 (42.02) |
| Analgesics           | 852 (14.90) |
| Antimalarials        | 640 (11.20) |
| Antibiotics          | 502 (8.80) |
| Antiallergens        | 159 (2.60) |
| Antacids             | 108 (1.90) |
| Hypnotics/Sedatives  | 104 (1.80) |
| Antifungals          | 100 (1.75) |
| Expectorants         | 99 (1.74) |
| Antisemics           | 58 (1.02) |
| Antihelminits        | 52 (0.91) |
| Myometrical Relaxants| 44 (0.77) |
| Anthypertensives     | 29 (0.51) |
| Others               | 559 (9.80) |

Other groups of medicines encountered included antihypertensives: methyldopa, 24 (82.8% of all antihypertensives presribed), nifedipine 4 (13.8%) and hydralazine 1 (3.5%). Hypnotics and sedatives encountered included diazepam 87 (83.7%), bromazepam 12 (11.5%), nitrazepam 5 (4.8%), antifungals (clotrimazole containing agents 65 (65%), tioconazole containing agents 24 (24%), nystatin containing agents 8 (8%) miconazole containing agents 3 (3%). Salbutamol 44 (0.77%) was also prescribed.

Majority of the medicines encountered were given orally 5268 (92.3%), others were by injectable route 336 (5.9%), per vaginal 99 (1.7%), instilling into the ears 2 (0.04%), eyes 1 (0.02%), anally 2(0.04%).

DISCUSSION

The average maternal age obtained in this study was similar to that obtained in a similar study in Nepal. Primigravid women formed the majority of women attending the antenatal clinics. The pattern of medical conditions obtained in this study varied with those reported in Nepal study where problem oriented drug use was mainly due to gastrointestinal tract problems (nausea and vomiting, dyspepsia), and vaginal spotting/ bleeding.

Malaria fever was the most prevalent medical condition occurring among the pregnant women in the antenatal clinics of the three health facilities. Malaria in pregnancy is a major public health problem in Nigeria, as well as other malaria endemic countries. Previous reports indicated that pregnant women attending ANCs perceived malaria as a common health problem. Malaria in pregnancy results in maternal anemia, intrauterine growth retardation, fetal low birth weight and neonatal mortality. The average number of drugs prescribed per encounter in the antenatal clinics differs from the standard set by WHO. However, similar values

Table 4: Risk classification of medicines and their frequency of occurrence (N=1200)

| Medicine             | Risk Classification |
|----------------------|---------------------|
| A                    | Adequate clinical studies have shown no risk to fetus in any trimester: Folic acid (671), Vitamin C (152), Vitamin B complex (104) |
| B                    | Animal studies have not shown adverse effect on the fetus and there are inadequate clinical studies: Paracetamol (749), Amoxycillin (110), Ampicillin/Cloxacillin (115), Metronidazole (59), Erythromycin (51), Cotrimoxazole (37) |
| C                    | Animal studies have shown adverse effects, no adequate clinical studies. May be useful in pregnancy despite potential risks: Codeine (54), Salbutamol (44), Methyldopa (24) |
| D                    | There is evidence of risk to human fetus, but potential benefits may be acceptable despite potential risks: Benzodiazepines (104), Dipyrone (96), Quinine (76), Aspirin (29) |
| X                    | Animal/human studies show foetal abnormalities. Risks involved clearly outweigh benefits: None |

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have been obtained in studies by Das et al.\textsuperscript{7} and Krause et al.\textsuperscript{17} The maximum number of drugs prescribed was 10. The high number may have resulted from prescribing routine drugs along with other medicines. The implication is that the patient may have more medicines than she can cope with in terms of cost and adherence. The high number may also increase the risk of adverse drug interactions. The total number of medicines obtained was more than that obtained by Gracia et al.\textsuperscript{18} but less than that obtained by Mengue et al.\textsuperscript{19} Most of the medicines were prescribed in brand names irrespective of the type, and this pattern is common in the country. The low value obtained on generic prescribing indicates that irrational prescribing occurred.

However value obtained by Das et al.\textsuperscript{7} was even lower. This means that prescribers here were not complying fully with WHO recommendation that drugs should be prescribed using their international nonproprietary names. The use of brand names may lead to increased cost of drugs for these women. Factors that may be responsible for this trend include the influence of drug promotional activities, pressures of pharmaceutical detail men, lack of continuing education on the principles of rational prescribing and non-familiarity with generic names among the prescribers.

The occurrence of injectables was low in this study, which is commendable since the use of injectables may introduce a high concentration of drug to the plasma, which could lead to toxicity in the pregnant women exposed. The percentage encounter of antibiotics was lower than that prescribed by WHO and this is encouraging.

The level of antimalarial prescription was low compared to the fact that malaria is endemic in this area. Such low level was also obtained in a previous study.\textsuperscript{10} This may have implication on the effectiveness of malaria intervention chemoprophylaxis programme.\textsuperscript{10} Prevention and treatment of malaria are essential components of antenatal care in endemic areas, but requires special considerations during pregnancy.\textsuperscript{14} Inadequate consumption of antimalarial drugs by patients may be a major contributing factor to the diminishing efficacy of the commonly available antimalarial drugs and development of drug-resistant strains of the P. falciparum malarial parasites in our community.\textsuperscript{14}

The occurrence of contraindicated medicines was low. Proper prescribing demands that such contraindications do not occur but the use of such medicines may be considered in cases where benefits outweigh the risk.\textsuperscript{20} Majority of the drugs prescribed were in category A of the FDA's classification of medicines according to risk to the foetus, followed by those in category B. However drugs in C and D were also obtained. This may have been in cases where benefits outweigh the risk. Similar results have been obtained in another study.\textsuperscript{19}

CONCLUSIONS
Malaria fever occurred most frequently followed by upper respiratory tract infections and gastrointestinal disturbances among the pregnant women. Minerals, vitamins and to a less extent antimalarials topped the list of the prescribed medicines. The average number of prescriptions per encounter was much higher than WHO standard, indicating occurrence of polypharmacy. The occurrence of contraindicated medicines was desirably low.

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CONFLICT OF INTEREST
None declared.

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