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# ANTI-MALARIA PRESCRIBING PATTERN IN MANAGEMENT OF MALARIA IN PREGNANCY IN TERTIARY INSTITUTION IN SOUTHERN NIGERIA

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## ABSTRACT

**Introduction:** Malaria infection during pregnancy is associated with poor maternal and fetal out comes.. Prompt and effective treatment, in accordance with recommended guidelines is essential to help prevent adverse events among mother and foetus. The Standard treatment guidelines for malaria states quinine and clindamycin as the drug of choice for treatment of uncomplicated malaria in first trimester and any of the following recommended artemisinin based combination therapies (ACT) for second and third trimesters. **Objective:** To evaluate the pattern of antimalarial prescriptions in all trimesters of pregnancy, at the University of Port Harcourt Teaching Hospital (UPTH). Also,to determine the level to which the prescription pattern comply with Standard guidelines. **Method:** A retrospective study of pregnant women (for all trimesters) treated for malaria between July 2018 - July 2020 in the University of Port Harcourt Teaching Hospital, was carried out. One hundred and three (103) patient case folders contained information regarding patient's malaria infection and treatment. Data collected includes: demographics information of patients; anti-malaria medications used; route of administration; other medications co-administered; presence of comorbidity; trimester of pregnancy in which malaria infection occurred. **Result:** The most frequently prescribed drug in the first trimester was Arthemeter (69%) and Arthemeter/lumefantrine 80/480mg (25%) and α-β artheeter (6%)**.** For the second and third trimesters Arthemeter i.m were the frequently prescribed, 56% and 52% respectively followed by Arthemeter/lumefantrine at 20% and 28%, α-β arteether 12%and 15% respectively and the least prescribed was the combination Arthemeter and the prophylactic drug Sulphadoxine-pyrimethamine for treatment at 12% and 5% respectively. **Conclusion:** The study carried out shows concerns in the antimalarial prescription pattern in the first trimester of pregnancy. While in the second and third the prescription pattern shows low conformity with the standard guidelines for treatment of malaria in pregnancy.

**KEYWORDS: P**rescription Pattern, Anti-malaria, Pregnancy.

## INTRODUCTION

Malaria is a life-threatening parasitic disease caused by an infectious bite of the female Anopheles mosquito but it is preventable and curable.[1] Malaria remains a major health problem in Nigeria affecting most children and pregnant women. Malaria infection during pregnancy has substantial risks for the pregnant woman, her fetus and the newborn child. For the pregnant woman, malaria infection can lead to severe disease and death, and placental sequestration of the parasite which can lead to maternal anaemia; it also puts the mother at increased risk of death before and after childbirth, and is an important contributor to stillbirth and preterm birth. Placental infection can also lead to poor fetal growth and low birthweight, which in turn can lead to child growth retardation and poor cognitive outcomes, as well as being a major risk factor for perinatal, neonatal and infant mortality.[2]

The five species of plasmodium that affect human are: *Plasmodium ovale*, *Plasmodium malariae*, *Plasmodium knowlesi*, *Plasmodium vivax*, *Plasmodium falciparum*. *Plasmodium falciparum* is the commonest species causing about 97% of uncomplicated malaria and it also the species most responsible for the severe form of the disease that leads to death in the country. *Plasmodium vivax* does not occur in indigenous Nigerians. Symptoms include fever, shivering, joint pains, headache, vomiting and in severe conditions, generalized convulsions and coma in severe cases. In malaria management, early diagnosis and prompt effective treatment is a vital component. Why are pregnant women especially at risk for malaria infection? Pregnant women are the most vulnerable group of malaria –associated morbidity and mortality. A pregnant woman has an increased risk of up to four times of getting malaria and twice the chances of dying from malaria, compared to a non-pregnant adult, because the immune system is partially suppressed

during pregnancy. Malaria in pregnancy, not only affects the mother but also has a dangerous sequel for the developing fetus, resulting in premature delivery or intrauterine growth retardation.[3,4] Pregnant women experience more bites as compared to non-pregnant women, which may be as a result of increased body surface and specific scents secreted during pregnancy.[5]

Placental malaria, malarial infection in placenta, is characterized by sequestration of *Plasmodium falciparum* infected erythrocytes and infiltration of immune cells within the intervillous spaces of the placenta. The placental turns black due to deposition of the malarial pigment. The parasite densities are much higher in the placenta compared to the peripheral blood. The thickening of the placental basement membrane, perivillous fibrinoid deposits, and syncytial knotting results into altered exchange system between mother and fetus. The placental in ability to supply sufficient nutrients to the fetus causes intrauterine growth restriction (IUGR) then increased vulnerability to infections during pregnancy results to high parasitemia and heavy infiltration of parasite infected RBC in placental vasculature, a good site where parasite can avoid maternal immune response. The severity of malarial infection in pregnant women also depends on prevalence of the infection in a particular community or area.[6] Prevention of malaria in pregnancy include intermittent preventive treatment therapy (IPTp). IPTp requires administration of an effective antimalarial drug sulfadoxine-pyrimethamine (each tablet containing 500mg/25 mg) to all pregnant women without testing whether or not they are infected with the malaria parasite, in all areas of moderate to high transmission. IPTp should be given at each routine antenatal care visit, starting as early as possible in the second trimester (thirteenth week) of pregnancy.

Pregnant women are routinely given folic acid supplementation to prevent neural tube defects in their infants. However, high doses of folic acid counteract the effect of sulfadoxine-pyrimethamine. Therefore, it is preferred that women take only the recommended 0.4 mg daily dose of folic acid. In some countries, 5 mg of folic acid are used, and in those countries, it is recommended to withhold folic acid supplementation for two weeks after taking IPTp with sulfadoxine-pyrimethamine to ensure optimal efficacy. Malaria can be diagnosed through clinical diagnosis, serology, molecular diagnosis, antigen detection, microscopic diagnosis. Effective case management remains a cornerstone for reduction of malaria morbidity and mortality. Prompt and effective treatment, in accordance with recommended guidelines is essential to help prevent adverse events among mother and foetus. The Standard treatment guidelines for malaria states quinine and clindamycin as the drug of choice for treatment of uncomplicated malaria in first trimester and any of the following recommended artemisinin based combination therapies (ACT) for second and third trimesters.[7]

Management of malaria in pregnancy is effective by combination of preventive measures which includes chemo-prophylaxis as well the use of drugs for the treatment of the condition. This study therefore aimed to determine the degree to which prescription pattern comply to the existing WHO treatment guidelines for malaria treatment among pregnant women. Also, to evaluate the pattern of antimalarial prescriptions in all three trimesters of pregnancy.

## METHOD

### Study setting

The study was carried out in the University of Port-Harcourt Teaching Hospital, Rivers State. Rivers state is located in South-Southern Nigeria made up of 23 local government areas. Its capital, Port-Harcourt, is the largest city with economic significance as the center of Nigeria's oil industry.

### Study design

A retrospective study was carried out on pregnant women who attended clinic in the Obstetrics & Gynaecology department between July 2018 to July 2020. The pregnant women who attended the clinic and had malaria that was treated were all recruited into the study.

Ethical approval was obtained from the University of Port Harcourt Teaching Hospital, Ethics Committee.

### Sample size

The sample size was determined with the following formula: (8)

$$n = \frac{Z_{1-a/2}^{2}\, p\,(1-p)}{d^{2}}$$

n =sample size; p = relative prevalence rate (50% or 0.5 which is maximum possible proportion; d = margin of error; Z = is the selected alpha level of 0.025 in each tail which is 1.96.

A sample size of 385 was obtained from the calculation and retrieved from the record Unit of the hospital. But 103 case files that had information on pregnant women who attended clinic at the Obstetrics and Gynecology department of University of Port Harcourt Teaching Hospital from July 2018 to July 2020 (24 months) who were infected with malaria and treated, were collected from the records department of the hospital.

Data extracted from the case files include: anti-malaria medication used;duration of treatment; route of administration; other medications co administered; co morbidity; age of patient; marital status; educational level and; occupation; Trimester of pregnancy in which the malaria affects. These data was extracted from patients' folders into a structured data recording form.

Data analysis was carried out with SPSS version 20, and p-value > 0.05 was considered as significant level.

**RESULTS**

The demographic data of the participants are shown in Table 1. Most 49(47.6%) of the study population were within 26yrs to 33yrs. Only 9(8.8%) were within 34yrs to 45yrs.

**Table 1: Demographic data of study Population.**

| SN | Variables | Frequency | Percentage |
|---|---|---|---|
| 1 | **Age** | | |
| | 18 to 25 years | 45 | 43.6% |
| | 26 to 33 years | 49 | 47.6% |
| | 34 to 45 years | 9 | 8.8% |
| | **Total** | **103** | **100** |
| 2 | **Marital Status** | | |
| | Single | 7 | 6.8% |
| | Married | 91 | 88.3% |
| | Widow | 3 | 2.9% |
| | Divorce | 2 | 1.9% |
| | **Total** | **103** | **100** |
| 3. | **Educational Qualification** | | |
| | Tertiary education | 12 | 11.7% |
| | Secondary education | 35 | 33.9% |
| | Primary education | 42 | 40.8% |
| | No formal education | 14 | 13.6% |
| 4. | **Occupation** | | |
| | Business | 46 | 44.7% |
| | Housewife | 15 | 14.6% |
| | Civil servant | 42 | 40.7% |
| | **Total** | **103** | **100** |

Source: Obstetrics and Gynecology department clinic record 2018-2020, University of Port Harcourt Teaching Hospital, 2021.

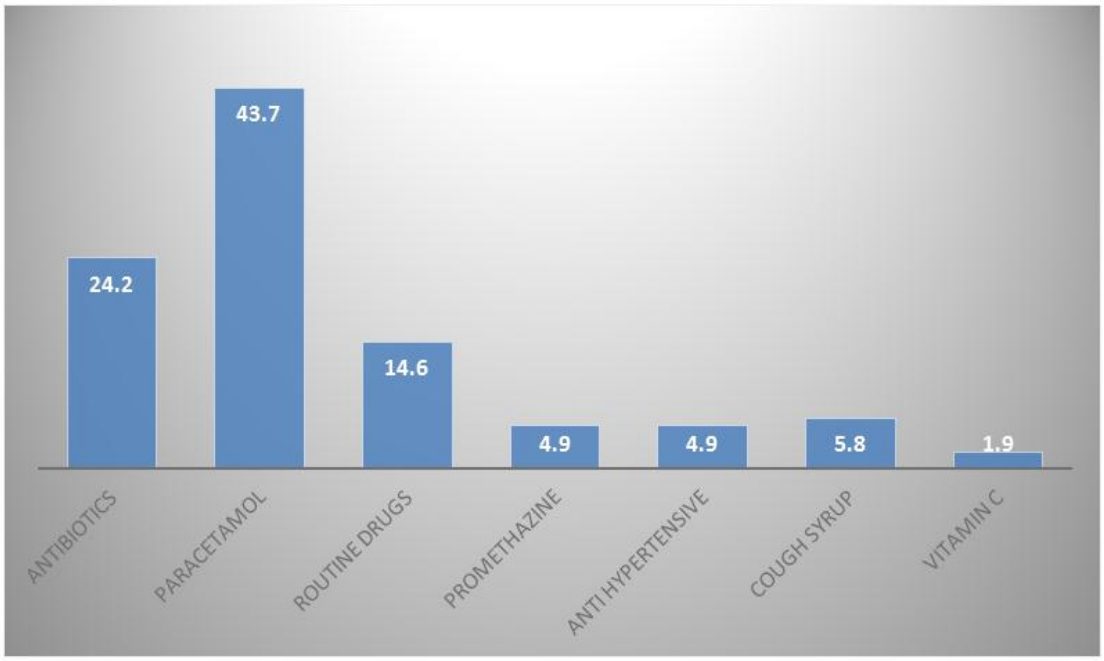


**Fig. 1: Shows Non-antimalarial drugs prescribed.**

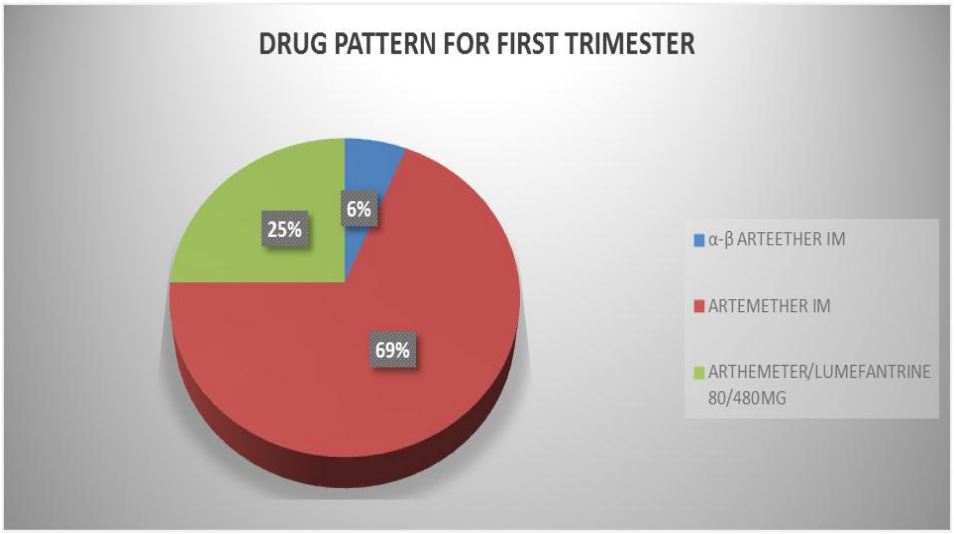


**Fig. 2: Shows the pattern of antimalarial prescription in all trimesters of pregnancy.**

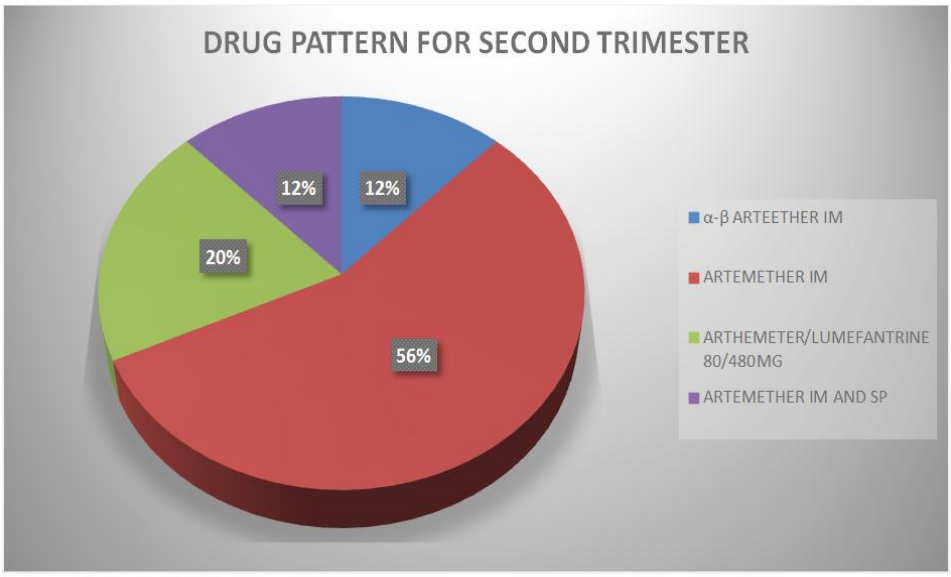


**Fig 3: Shows prescription pattern for antimalarial use in second trimester of pregnancy.**

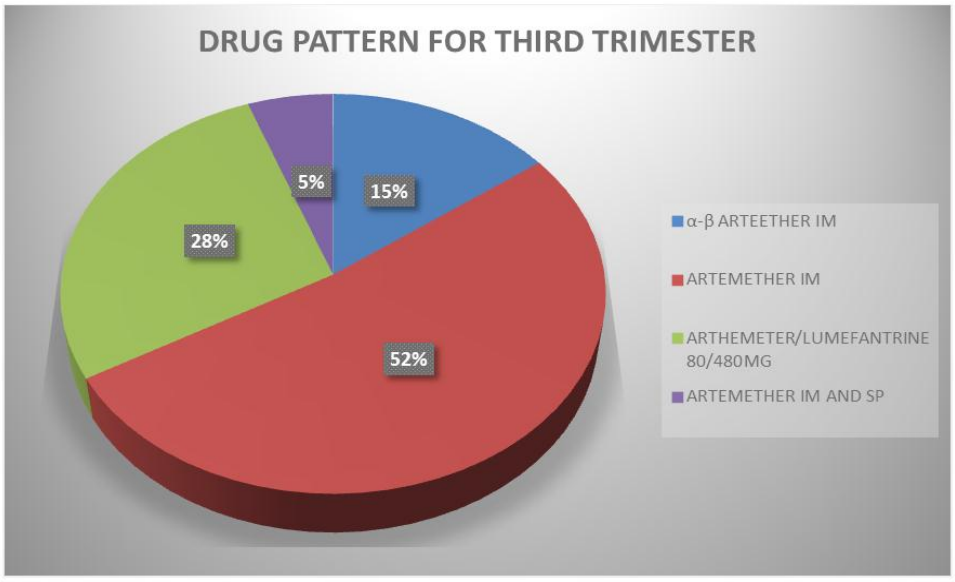


**Fig 4: Shows prescription patterns of antimalarial for third trimester of pregnancy.**

The result of antimalarial prescription pattern for first, second and third trimesters are shown in Figs 2, Fig 3 and Fig 4. In first trimester, arthemeter intramuscular (im) injection was mostly used in each of the three trimesters and α-β arthemeter im was the least prescribed in all the trimesters

**SECOND TRIMESTER**

**Table 2: Patients access to use of IPTp.**

| | Frequency | Percent % | Valid Percent | Cumulative Percent |
|---|---|---|---|---|
| Did not access IPTp | 12 | 42.9 | 42.9 | 42.9 |
| Accessed IPTp | 16 | 57.1 | 57.1 | 100.0 |
| System Total | | | 100.0 | |
| | | | | |
| Total | 28 | 100.0 | | |
| **THIRD TRIMESTER** | | | | |
| | **Frequency** | **Percent %** | **Valid Percent** | **Cumulative Percent** |
| Did not access IPTp | 22 | 38.6 | 38.6 | 38.6 |
| accessed IPTP | 35 | 61.4 | 61.4 | 100.0 |
| Total | 57 | 100.0 | 100.0 | |

**DISCUSSION**

From data on non-antimalarial drug administration, the highest drug administered in combination with the malaria drug was paracetamol at 45 (43.7 %), while the lowest drug administered in combination with the malaria drug was vitamin C, giving paracetamol (acetaminophen) to patients ill with severe malaria made them less likely to develop potentially fatal kidney failure.[9,10] reported that giving regular doses of paracetamol protects the kidney in adult patients with severe falciparum malaria. Each year severe malaria causes close to half a million deaths globally. Acute kidney injury (AKI) complicating severe malaria is an important cause for death. AKI occurs in 40 % of adults and at least 10 % of children with severe malaria, killing an estimated 40 % of these adults and 12-24 % of the children. This is an important finding, because acute kidney injury is a very common, often fatal complication in adult patients with severe malaria. More so the low administration of vitamin C in our research is not unrelated to a study from Nigeria involving 80 malaria infected adult patients[11] illustrate that co-administration of orange juice, grapefruit juice or vitamin C concomitant with artesunate or artemether severely diminishes the efficacy and potency of these widely used therapy.

Routine drugs such as; Folate (vitamin B9) is an essential nutrient that is required for DNA replication and as a substrate for a range of enzymatic reactions involved in amino acid synthesis and vitamin metabolism. Demands for folate increase during pregnancy because it is also required for growth and development of the fetus. Folate deficiency has been associated with abnormalities in both mothers (anemia, peripheral neuropathy) and fetuses (congenital abnormalities).[12] However high doses of folic acid should not be administered together with sulphadoxine-pyrimethamine, promethazine for treating emesis, antihypertensive drugs such as nifedipine and methyl dopa. And antibiotics for treatment of bacterial infection.

Urinary tract infection was a major comorbidity associated with malaria in pregnancy, urinary tract is common in pregnancy and this is due to the increased production of pregnancy hormone. Decreased estrogen levels cause changes in the vaginal flora and increase in the colonization of bacteria, increased Progesterone relaxes the ureter muscles thereby slowing down the voiding of urine and flow leading to infection. Also as the uterus grows there is mechanical compression of the urinary tract.[13] The co prescribed drug for this was antibiotics such as nalidixic acid.

Pattern of antimalarial prescription in all trimesters of pregnancy.

Hospital data on the pattern of antimalarial prescription in the first trimester depicted (69.0%) of patient were administered Artemether IM (arthemisinin derivatives), while (25.0%) were administered Artemeter/lumefantrine 80/480mg, and (6%) were administered α-β arteether. data on the pattern of antimalarial prescription in the second trimester depicted (56.0%) of patient were administered artemether IM, (20.0%) were administered artemeter/lumefantrine 80/480mg while (12.0%) were administered artemether IM and sulfadoxine-pyrimethamine, 12% were administered α-β arteether. In contrast data on the pattern of antimalarial prescription in the third trimester depicted (52.0%) of patient were administered Artemether IM while (28.0%) were administered Artemeter/lumefantrine 80/480mg, while (5.0%) were administered artemether IM and sulfadoxine-pyrimethamine, and (15%) were administered α-β arteether. The high rate of prescription of Artemether IM compared to other medication in the study is in consonant with the reviewed works by Khalid et. al.,[14] This review revealed that most of the revised national guidelines/PMI-MOP reports are non-compliant to WHO Guidelines recommendations. They opined that artemether is an alternative artemisinin-based medicine but is only available as a pre-mixed oil-based solution for intramuscular injection, it is now widely available and is used in many African countries, in adults artemether is

probably more effective than quinine at preventing deaths. With respect to other patient-oriented outcomes such as fever and parasite clearance time, artemether seems to be more effective than quinine in children and adults. For adults, artemether had a large effect on death compared to quinine. Artemether has not been compared to artesunate in children. Although there is a paucity of direct evidence comparing artemether with artesunate in adults, artemether probably increases the risk of death compared to artesunate. In settings where artesunate is not available, artemether remains a better alternative to quinine for the treatment of severe cases.

Assessing the extent to which prescription pattern adhere to the WHO treatment guidelines

ACTs are not recommended for malaria in the first trimester of pregnancy. This is due to the national policy for malaria in pregnancy which does not approve ACTs as first choice medicines in early pregnancy because it put unborn babies at risk of adverse effects, it can only be administered when they are the only treatment available, or in a case were the patient's life is threatened. The use of ACT in second and third trimester of pregnancy found no association between ACT treatment and congenital malformations.

Data collected in assessing the extent to which prescription pattern adhere to the WHO treatment guidelines for controlling malaria and its effects during pregnancy, in the second trimester 12 (42.9%) of pregnant women did not access intermittent preventive treatment, while 16 (57.1%) had access to it, however in the third trimester 22 (38.6%) of pregnant women did not access intermittent preventive treatment, whereas 35(61.4%) had access to intermittent preventive treatment, from the result it was inferred that a large proportion of pregnant women did access intermittent preventive treatment as prescribe by the WHO (2003), they posit that prevention and treatment of malaria during pregnancy is crucial for reduction of parasitaemia and improving birth outcome, possible efforts should be made to increase access to medication in areas with moderate to high malaria transmission in Africa, as part of antenatal care services.[15,16] WHO recommends a schedule of at least three antenatal care visits during pregnancy, starting as early as possible in the second trimester, it recommend intermittent preventive treatment in all pregnant women at each scheduled antenatal care (ANC) visit until the time of delivery, provided that the doses are given at least one month apart. The International Roll Back Malaria (2014) initiative recommended three cost effective protective measures for all pregnant women, which are use of intermittent preventive treatment, insecticide-treated mosquito nets and effective case management of malarial illnesses.

## CONCLUSION

The pattern of antimalarial prescription in the University of Port Harcourt Teaching Hospital varied and conformed poorly to the evidence based national policy on malaria control in the first trimester, and low conformity in second and third trimesters. The practice of prescribing outside the current guidelines should be addressed through comprehensive training and continuing professional development to keep professionals up to date with current trends in malaria treatment during pregnancy and increased supportive supervision.

### Limitations of study

The study was intended to asses a larger number of patients but a lower number was available for access. This was found to be as a result of inappropriate documentation and data management as some folders were missing in records department offices, making it difficult to access such folders as well as patients in their first trimester failing to register for antenatal program early in pregnancy. According to the world health organization on antenatal care, pregnant women are to have the first contact with health care providers in the first 12 weeks of gestation, with subsequent contact taking place at 20, 26,30,36,38 and 40 weeks gestation. (WHO recommendation on antenatal care., 2017)

### Recommendations

A proper and comprehensive data management system should be implemented to enable ease of research

Creating awareness on the need to register early for the antenatal care services

Provision of a structured and planned system for continuous education for health practitioners.

Increased supportive supervision for health care practitioners

### Conflict of interest

The authors declared no conflict of interest.

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