

Antenatal Care in Sao Tome and Principe: Beyond the Number of Visits

Alexandra Vasconcelos (✉ alexandravasc@gmail.com)

Universidade Nova de Lisboa Instituto de Higiene e Medicina Tropical <https://orcid.org/0000-0001-8042-0846>

Swasilanne Sousa

Hospital Dr. Ayres de Menezes, São Tomé e Príncipe

Nelson Bandeira

Hospital Dr. Ayres de Menezes, São Tomé e Príncipe

Elizabeth Carvalho

PMI_São Tomé e Príncipe Ministry of Health

Marta Alves

NOVA University of Lisbon: Universidade Nova de Lisboa

Ana Luísa Papoila

NOVA University of Lisbon: Universidade Nova de Lisboa

Maria do Céu Machado

Universidade de Lisboa Faculdade de Medicina

Filomena Pereira

Universidade Nova de Lisboa Instituto de Higiene e Medicina Tropical

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Abstract

Background: Newborn mortality in Sao Tome and Principe (STP) is overwhelmingly high and the antenatal healthcare (ANC) is one of the strategies to achieve its reduction. This study aimed to know which antenatal screenings are done in STP and which antenatal problems are detected.

Methods: A retrospective study in which 518 pregnant women antenatal cards were reviewed between July 2016 and November 2018. Information analysed included clinical factors, laboratory tests, ultrasounds, results, and treatment.

Results: Mothers' mean age was 26.6 (SD=7.1) years old. At least one ANC visit occurred in 98.6% pregnant women and 38.7% had 8 or more. Regarding laboratory screenings, blood group was done in 64.4%, haemoglobin tested in 62.5% (first trimester) and in 29.3% (second trimester) and, urine once in 57.1% and twice in 12.2%. Antenatal problems identified in the pregnant women studied were: i) a RhD-negative phenotype (5.8%); 2) anaemia 1st trimester (36.4%) and 2nd trimester (35.5%); 3) bacteriuria (43.2%); 4) intestinal parasites (55.5%); 5) sickle cell solubility test positive (13%). Overall, 161 (53.7%) out of the 300 ultrasounds were done before the 20th week.

Conclusion: In Sao Tome and Principe many pregnant women do not have access to the full spectrum of ANC recommended screenings. Maternal anaemia and bacteriuria are the main health problems that should be urgently addressed to prevent newborn morbidity and mortality in the country. Other preventive interventions as anthelmintic drugs should be debated as intestinal parasites were diagnosed in more than half of the women. Alloimmunization to RhD is also a concern due to the unaffordability of anti-D immunoglobulin in the country.

Plain English Summary

Access to quality antenatal healthcare care (ANC) is one of the most effective means of reducing neonatal mortality. Sao Tome and Principe has an overwhelmingly high neonatal mortality rate, so we aimed to describe current antenatal care practices in the country.

Most studies about ANC in Sub-Saharan countries analyse it into utilized and not utilized (only based on the total number of visits) or timing of first ANC attendance. In the present study we decided to go further on and assess screenings performed (obstetric ultrasound, haemoglobin, and urine tests), in addition to the number of attendances. The main antenatal problems and diseases were also analysed. Hence, detecting main vulnerabilities of antenatal care practices in the country can provide some clues on how to improve newborn outcomes and health through optimising ANC. We intended to contribute with this study to the development of a strategy to improve maternal and newborn health as endorsed in the post-2015 Sustainable Development Goals.

Background

Antenatal care (ANC) was a concept created in the early decades of the past century, that is now widely acknowledged for its potential for improving newborn survival and health [1, 2, 3] as it is an excellent opportunity to reach pregnant women with prophylactic medication, vaccines, diagnosis, and treatment of infectious diseases, as well as with health education programs [4, 5, 6]. A variety of ANC models are currently available for low-resource contexts, however, content and quality of antenatal care received by pregnant women varies tremendously due to factors both related to nations health policies, facilities and to users [2, 9, 10, 11, 12].

The World Health Organization (WHO) recommendations on “antenatal care for a positive pregnancy experience” state that adequate ANC should start early for timely detection and treatment of maternal problems to reduce complications during pregnancy, childbirth, and puerperium with a goal of a minimum of eight contacts per pregnant women [7, 8].

Main essential evidence-based screenings preconized by the WHO include assessment of maternal anaemia, asymptomatic bacteriuria, gestational diabetes, human immunodeficiency virus (HIV), tuberculosis, and syphilis [13]. For foetal assessment, an ultrasound is recommended before week 24 to identify multiple gestation, congenital anomalies, estimate gestational age, foetal malpresentation and placenta praevia [14, 15] as it is the most accurate non-invasive screening tool. Unfortunately, obstetric ultrasound is not widely available in most Low-to-Middle-Income Country (LMIC) [14, 15].

Pregnant women should also be tested for human immunodeficiency virus (HIV), syphilis and hepatitis B (HBSAg) at least once during pregnancy, preferably in the first trimester [16]. Mother to child transmission of HIV ranges from 15–45% but it can be lowered to less than 5% with testing and initiation of antiretroviral treatments [17]. Syphilis, not treated properly, can likewise cause adverse pregnancy outcomes in about half of the cases—deaths and neonatal morbidity in 20%, small birth weight deliveries in 20% and stillbirths in 40% [18]; co-infection might also increase the risk of mother-to-child transmission of HIV.

Routine ANC laboratory tests are aimed to prevent maternal anaemia, puerperal sepsis, preterm birth, reduce the risk of stillbirths, of low-birthweight (LBW) and small-for-gestational-age neonates. Anaemia in pregnant women, for instance, is a major setback in newborn health as it relates to intrauterine growth retardation, preterm delivery, low birth weight, and foetal death [19]. Asymptomatic urinary tract infections in pregnancy, when it is not treated, it is associated with 30% risk of developing pyelonephritis, with subsequent probability of LBW and/or preterm delivery [20, 21]. These infections are extremely common during pregnancy because the short urethra in women makes the urinary tract to be easily contaminated with faecal flora [21].

Typhoid fever, caused by *Salmonella typhi*, is one of the most common bacterial causes of acute febrile illness in the developing world and may be a source of significant morbidity and mortality in both the mother and foetus [22, 23].

In sub-Saharan Africa, pregnant women with sickle cell disease (SCD) go often undiagnosed and have increased risks of acute painful episodes and pregnancy complications as foetal loss, intrauterine growth restriction, eclampsia, and preeclampsia [24]. On the other hand, the high prevalence of this undiagnosed non-communicable disease contributes to excess mortality in children under five years in Africa [24].

Antenatal prophylaxis with anti-D immunoglobulin in non-sensitized Rh-negative women at 28 and 34 weeks of gestation is not available in most Sub-Saharan African countries [25]. Alloimmunization prevention following potentially sensitizing events and during medical termination of pregnancy in Rh-negative women reduces perinatal adverse outcomes of the foetus and newborn during a second RhD-positive pregnancy. In its mildest form the newborn has sensitized red blood cells, however, the haemolytic disease may result in intrauterine death or newborn jaundice, anaemia, and infant developmental problems [26].

Sao Tome and Principe (STP), the second smallest Sub-Saharan country, has high levels of neonatal mortality, high levels of poverty, a lack of skilled medical personnel and a lack of health infrastructure that can be main obstacles to adequate skilled maternal health care [27, 28, 29].

Although the considerable progress in the country for maternal mortality ratio, from 158.3 maternal deaths per 100,000 live births in 2009 to 74 maternal deaths per 100,000 live births in 2014, neonatal mortality and morbidity is increasing, as each year, around 22 newborn babies die per 1000 live births and there are 22 stillbirths per 1000 live births, representing a major public health problem [27, 28, 29].

Many authors have studied the ANC in Africa and their determinants, but few have investigated the quality of the services through preconized interventions and screenings performed [1–4, 7–11].

Hence, looking at the current antenatal care practices in the country – attendance and evidence-based screenings – we aim to provide some clues on how to improve newborn outcomes by optimising ANC [1, 9, 11, 30, 31, 32, 33, 34, 35]. To the authors' knowledge no study on this subject has been performed in Sao Tome and Principe.

Material And Methods

Study design

An institution-based retrospective study was conducted between July 2016 to November 2018.

Study context

The archipelago of Democratic Republic of Sao Tome and Principe has two islands, with a total land surface of around 1,001 km², 859 km² of which for Sao Tome and 142 km² for Principe. The country has no land borders, but lies relatively close to the coasts of Gabon, Equatorial Guinea, Cameroon, and Nigeria. STP level of poverty is high, 66.2% of the population lives on less than 1.40 United States Dollar (USD) per day, considered to be a major obstacle to achieve universal coverage [29]. Antenatal

consultations are free, but each woman pay around 6.7 USD for all mandatory tests (blood, urine, faeces, gynaecological exams). Obstetric ultrasounds are around 10 USD and are mainly available at private obstetricians' clinical facilities [29].

There are six basic obstetric services with the capability of performing ultrasound available in the rural districts. Complete obstetric services are only available at the only hospital in the island, Hospital Dr. Ayres de Menezes (HAM) that has a maternity unit responsible for 82,4% of all the deliveries in the country [29].

In STP antenatal care is available to women on all working days. Antenatal care visits are carried out by nurses. They are normally organized along the five thematic components of service provision stipulated by the WHO guidelines: 1) history taking, 2) physical examination, 3) laboratory examinations, 4) drug administration and immunization and 5) health education [13]. Routine ANC includes measurement of blood pressure, iron supplementation, tetanus-diphtheria injections blood tests (haemoglobin, blood group, Rhesus factor, hepatitis B surface antigen, sexually transmitted infections), urine tests, stool tests and anthelmintic drug therapy [13] [29].

Screening of human immunodeficiency virus (Determine© test), hepatitis B virus (hepatitis B surface antigen - HBsAg) and syphilis (rapid plasma reagin test) are included in the STP's essential package of interventions for maternal and newborn health, which is done using an opt-out approach and are free of charge [29]. Other essential laboratory tests, rapid tests and ultrasounds have costs for the pregnant women.

Midstream urine culture (the gold standard) is the recommended method for diagnosing asymptomatic bacteriuria, but urine culture is not available, so urine dipstick test in health posts and laboratory urine in other centres are the used method [13].

The glucose level should be measured along pregnancy. According to WHO criteria, blood sugar levels are recommended to be checked at least twice, before and after the 20th pregnancy week [13].

As full blood count testing is not available, on-site haemoglobin testing is performed with a haemoglobinometer. The full blood count testing gold-standard recommended method for diagnosing anaemia in pregnancy is only available at HAM [13, 19]. The guidelines recommend that haemoglobin should be measured at the first visit and, if normal, measured again at 28–32 weeks and 36 weeks [29].

Blood culture is commonly used as the reference standard for typhoid diagnosis but requires sophisticated equipment not readily available in most LMIC as in STP [36]. The Widal test is a quantitative agglutination test that identifies serum antibodies against Salmonella antigens O-somatic and H-flagellar and in STP it is routinely performed once during pregnancy, regardless of the existence of any clinical suspicion [23]. The test is considered positive if a convalescent phase serum sample has a fourfold higher titer than an acute sample [23].

A sickle cell solubility test, which involves treating a thin blood film with sodium dithionite under hypoxic conditions and observing for sickling under a light microscope, is the screening technique available in STP and performed to pregnant women with anaemia or clinical suspicion [37, 38]. A positive result can suggest either sickle cell anaemia or the sickle cell trait [37]. The diagnosis of sickle cell disease cannot be established with certainty by means of the sickling test alone, but must be substantiated by electrophoretic analysis, unfortunately not available in the country [38].

ANC cards or pregnancy bulletin are an important working tool. In Sao Tome and Principe, it has 10 pages and health workers use them as a continuous pregnant women documentation registering personal information, physical examinations, laboratory tests, treatments, and other notes. Pregnant women bring the card to each visit and to the maternity ward at the time of delivery.

Eligibility criteria

All women admitted to the hospital for delivery with a gestational age of 24 weeks or more were eligible to be enrolled in the study. Those who gave birth outside the hospital but were admitted for postnatal complications were also included in the study. Pregnant women without antenatal cards were excluded.

Study population and sampling

Women who delivered at HAM during the study period (July 2016 to November 2018). Mothers were selected by convenience sampling. Five hundred and eighteen antenatal care cards were reviewed.

The software used for sample calculation was Raosoft (<http://www.raosoft.com/samplesize.html>), but this value was supported by PASS software (<https://www.ncss.com/software/pass/>). There was a mean of 4540 HAM deliveries/year within the study period. The sample size was calculated based on a minimum sample of 10% of the population validated by the sample calculation software, which placed the right dimension between 355 (95%) and 579 (99%) confidence. It was possible to collect 518, which gave some comfort at this level.

Data collection

Antenatal care card of each study participant was used to collect personal data, obstetric and pregnancy follow-up information. The main investigator was responsible for all data collection and review.

The information was collected on mothers' age, place of residence, educational status, occupation; obstetrics characteristics such as: parity, gravidity, history of abortion and stillbirth, timing at first ANC booking, presence of maternal medical disease (e.g. chronic hypertension, diabetes mellitus, asthma and anaemia); clinical conditions observed during gestation - urinary infections at any point during pregnancy, syphilis, HIV, hepatitis B; and risky behaviours as alcohol consumption, smoking, drug use and also presence of domestic violence during pregnancy.

Employment was defined as employed for those who engaged in one economic activity or another and not employed for those who did not engage in economic activities. Residence was grouped into urban

and rural. Urban area was considered to be living in Água Grande district and rural areas in Mé-Zochi, Cantagalo, Lobata, Lembá, Caué and Príncipe Island.

Gravidity was categorized as primigravida (1), multigravida (2–4) and grandmultigravida (above 5). Parity was classified as nulliparous (1), multiparous (2–4) and grandmultigravida (above 5).

In addition, data were gathered following 2016 WHO guideline recommendations: nutritional interventions as daily oral iron and folic acid supplementation (A.); maternal assessment with on-site haemoglobin testing for diagnosing anaemia in pregnancy and urine tests (B.1), HIV and syphilis screening (B.1.7); foetal assessment (B.2) with one ultrasound scan before 24 weeks of gestation (early ultrasound) (B.2.4); preventive measures (C.). [13] Antenatal care models with a minimum of eight contacts as recommended to reduce perinatal mortality and improve women's experience of care (E.7) [13].

These evidence-based interventions were also described and grouped according to the number of antenatal care attendances: 1–3, 4 to 7 visits and 8 or more. The interventions were divided in once or twice tested for HIV, syphilis, HVB, malaria, hemoglobin, urine test and stool exam. The pregnancy week of first antenatal care attendance (before or after the 16th), blood group and obstetric ultrasound were also analyzed.

Data management and statistical analysis

Data were held in a confidential and private location. Participants were referred to by identification numbers and the informed consent forms were kept separate from the questionnaires. Both could only be linked by a coding sheet available only to the investigators. Characteristics of study participants were described with frequencies (percentages) and with median and inter-quartile range (IQR: 25th percentile–75th percentile) or range (min-max), as appropriate. Data were entered in QuickTapSurvey (©2010–2021 Formstack) and the dataset exported to Excel for cleaning and further analysis in the Statistical Package for the Social Sciences for Windows, version 25.0 (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.).

Ethics approval and consent to participate

Approval to carry out this study was obtained from the Democratic Republic of Sao Tome and Principe Ministry of Health ethics committee and Hospital Ayres de Menezes. Written informed consent was obtained from all participants (or their parent or legal guardian in the case of teenage under 16) after the purpose of the research was explained orally by the investigator. This was done only after delivery to assure a labour without fear of punishment or feelings of coercion. Participation in the survey was voluntary, as participants could decline to participate at any time during the study. Anonymity of participants was ensured.

Results

Pregnant women's socio-demographic characteristics

The maternal socio-demographic characteristics of the 518 women analysed indicated that mother's mean age of the current pregnancy was 26.6 (7.1) years old, between 14 and 43 years of age. Twenty-eight (5.4%) were aged between 14 and 16, 14.7% (76) 17 - 19, 63.1% (327) 20 - 34 years and 16.8% (87) were older than 35 years of age. Regarding mother's education, 58.5% (303) had primary education and 31.7% (164) had a secondary education. Higher education was found in 6.3% (33) with 4.2% (22) achieving a higher education degree. Illiteracy was found in 3.5% (18). Concerning employment status, 64.2% (330) were not employed, 28.3% (147) were employed and 7.2% (37) were students. Urban area living was confirmed in 45% (233), while 53.1% (275) were living in rural areas, such as Mé-Zochi 28.4% (147), Cantagalo 11.2% (58), Lobata 6.2% (32), Lembá 4.2% (22), Caué 1.7% (9) and Principe Island 1.4% (7).

Antenatal care

Concerning ANC attendance, 98.6% (511) of the pregnant women attended the antenatal care facilities at least once. Regarding the number of antenatal visits, 14.9% (76) had less than 4 visits, 46.4% (237) had 4 to 7 attendances and 38.7% had complete ANC (≥ 8 visits). The mean gestational age at which the study participants initiated ANC visit was 12.9 (5.6) weeks. The detailed distribution of gestational age at initiation of ANC attendance is shown in Fig. 1. While most of the mothers started ANC visit in the first trimester of gestation corresponding to 51.7% (268), 31.5% (163) and 2.9% (15) initiated ANC visit in the second and third trimesters respectively. A total of 71.4% (370) attended before the 16th week of pregnancy.

Pre-pregnancy characteristics

Pregnant women's age as a risk factor was recorded in 22% (115) of ANC cards: adolescent pregnancy (≤ 16 years old) in 5.4% (28) and 16.8% (87) higher than 35 years old. Notification of a high-risk pregnancy in 30% (161) of cases. Family medical history was recorded in two cards (0.38%). Maternal disease was notified in 11.2% (58) of the cards; 2.3% (12) reported chronic hypertension, 2.5% (13) allergic conditions, 1.4% (7) asthma, 1.4% (7) recurrent urinary tract infection, 0.6% (3) diabetes and 0.6% (3) sickle cell disease. Primigravida, multigravida and grandmultigravida were found in 24.5% (127), 51.7% (268) and 23.7% (123), respectively. Nulliparous, multiparous and grandmultigravida were observed in 29.3% (152), 60.8% (315) and 9.8% (51) respectively. About 29.9% (155) had prior history of miscarriages and 3.9% (20) of stillbirths, although no more details were specified in their ANC cards. Whether the pregnancy was planned or not was documented on 3 cards (0.57%). Former contraception was recorded in 10 (1.9%) women. Presence of domestic violence during pregnancy was recorded in three women, alcohol consumption in four. None was signalled to have other risky behaviours as smoking or drug use (cocaine, crack, marijuana) during pregnancy.

Physical examination and pregnancy complications

Routine measurement of height, weight, foetal heart rate that should be carried out by nurses were not found registered in any antenatal card. Blood pressure was registered in 80%. Preeclampsia was detected during ANC visits in 7.1% (37). First-trimester bleeding was reported in 0.2% (1), second-trimester in 0.2% (1) and 1.2% (6) experienced third-trimester bleeding. All preeclampsia and bleeding were referral to the main maternity for further evaluation.

Laboratory tests and immunization/drugs

Blood group tests were done in 64.4% (334) and revealed that 17.4% (58/334) were group A, 26.3% (88/334) group B, 54.7% (183/334) group O and 1.6% (5/334) were group AB. Rhesus factor was done by 62.9% (326) being positive in 94.2% (307) while 5.8% (19) were Rh negative. None received antenatal prophylaxis with anti-D immunoglobulin.

Screening for HIV was done in 94.2% (488/518) of cases, 41.1% (213) performed one test and 53.1% (275) two tests, with a positive test in 4 (0.8%). Syphilis screening was done in 89.9% (466) of women, 88.8% (460) performed one rapid test and 1.2% (6) had two tests. A total of five tests (1%) were positive and these women received treatment. Hepatitis B screening was done once in 59.8% (310) and twice in 0.2% (1). Hepatitis B was diagnosed in 5.8% (18/310) and 5 had syphilis (2 non-treated before hospital admission).

Malaria screening was done in 73% (379) with one-time test in 66% (342) and two tests in 7.1% (37). Malaria was detected in three (0.8%) pregnant women. Administration of one dose of Sulphadoxine-Pyrimethamine for intermittent preventive treatment for malaria during pregnancy (IPTp) was given to 46.7% (242) of women, 42.5% (220) received two doses and 4.2% (22) had none. Insecticide Treated Nets (ITN) were delivered to 85.3% (442) of them.

Haemoglobin testing before the 20th gestational week was performed in 62.5% (324), from which anaemia was detected in 36.4% (118/324). Haemoglobin test after the 20th gestational week was done in 29.3% (152), from which anaemia was detected in 35.5% (54/152). Lack of economic support in 35.5% (184) and lack of reagents in 2% (10) were the reasons registered in their antenatal cards. Iron/folate tablets were prescribed to 85.7% (444).

Blood glucose test before the 20th pregnancy week was done in 53.8% (279) of women, with 3.6% (10) having high values (≥ 105 mg/dL). After the 20th week blood glucose was tested in 17.4% (90) with 6.7% (6/90) having high values. The test was not performed in 46.2% (239) before the 20th week and in 82.6% (428) after the 20th week.

Urine tests were done in 69% (359), with 57.1% (296) performing one test and 12.2% (63) two tests. A total of 43.2% (155/359) had a positive urine test and 62.5% (97/155) were treated with an antibiotic: 92.7% (90/97) with amoxicillin, 5.5% (5/97) ampicillin and 2% (2/97) with cefotaxime.

Intestinal parasites testing with thick stool samples smears (prepared and assessed using the Kato-Katz technique) was done in 71% (369), one test in 63.5% (329) and two in 7.7% (40). Out of a total of 55.5% (205/369) of pregnant women who had their first stool test positive, 24.4% (50/205) were treated, while 31.3% (5/16) of 40% (16/40) that had the second test positive received treatment. Albendazole was given in 10.2% (21/205) and 18.7% (3/16) respectively, mebendazole in 9.2% (19/205) and 12.5% (2/16), metronidazole in 2.9% (6/205) and 12.5% (2/16) and piperazine in 1.5% (3/205).

Vaginal smears were performed in 67.7% (351), one test in 61.8% (320) and two in 6% (31). *Candida albicans* was detected in 53.3% (104/195).

Sickle solubility test for detection of sickle cell anaemia and sickle cell trait was done by 54.8% (284) of the pregnant women with 13% (37/284) having a positive test.

Widal test was offered once to 45.6% (236) with 14.8% (35/236) considered to be positive. There was no information in their ANC cards regarding associated clinical symptoms nor antibiotic treatment prescribed.

Regarding immunization, 93.4% (483) had received tetanus toxoid immunization 1.9% (9/483) had one dose, 32.1% (155/483) had two, 23.6% (114/483) had three, 18% (87/483) had four and 24.4% (118/483) had the complete five doses. In 3.5% (18) of the antenatal cards, no dose was registered.

Obstetric ultrasound

Obstetric ultrasound was done in 57.9% (300), 53.7% (161) being before the 20th week of pregnancy. Follow-up by ultrasound was done once in 41.7% (216), twice in 13.9% (72), three times in 2.3% (12) and four times in 0.2% (1). From a total of 3,1% (17) of twin pregnancies, 2.8% (15) were confirmed by ultrasound. Major congenital malformations were identified in two fetuses.

Evidence-based interventions

Evidence-based interventions are described in Table 1, 2 and 3 according to number of ANC visits: 1 to 3 (inadequate ANC attendance), 4 to 7 (adequate ANC) and 8 or above (complete ANC), respectively.

First ANC attendance before the 16th week (early ANC) was observed in 77.2% and 93.1% of the pregnant women with 4-7 ANC visits and with 8 or more, respectively. Two HIV screenings were done by 26.3% in those with 1-3 visits, 53.4% for those with 4-7 and 65.5% for those with 8 or more ANC visits. Two syphilis screenings were observed in 0.9% of pregnant women with 4-7 visits and 2% of 8 or more visits.

Regarding two haemoglobin and urine tests for women with 1-3 visits were 2.6% and none respectively. For pregnant women with 4-7 visits 10.5% had two haemoglobin tests and 7.2% performed two urine tests. Regarding those with 8 or more ANC visits 31.8% had two haemoglobin tests and 23.2% had two urine tests. Obstetric ultrasound before the 20th pregnancy week was observed in 7.9%, 27.8% and 44.9% according to 1-3 ANC visits, 4-7 and 8 or more.

Table 1. Adequacy of use of evidence-based interventions according to ANC (antenatal care) number of visits 1 to 3 (inadequate ANC attendance)

| Screenings | ANC visits 1-3 (Inadequate ANC) | |
|---|--|------------------------|
| | n=76 (14.9%) | |
| First ANC attendance | >16 th week | <16 th week |
| | | 31/55 (56.4%) |
| Blood group | 24 (31.6%) | |
| | 1 test | 2 tests |
| HIV | 52 (68.4%) | 20 (26.3%) |
| Syphilis | 69/75 (92.0%) | 0 |
| Hepatitis B | 47/75 (62.7%) | 0 |
| Malaria | 24 (31.6%) | 1 (1.3%) |
| Urine dipstick | 27/75 (36.0%) | 0 |
| Stool exam | 24 (31.6%) | 0 |
| Haemoglobin test | 24 (31.6%) | 2 (2.6%) |
| Timing of the haemoglobin test | < 20 th week | >20 th week |
| | 20 (26.3%) | 8 (10.5%) |
| Ultrasound | | |
| 0 | 60 (78.9%) | |
| 1 | 13 (17.1%) | |
| 2 | 2 (2.6%) | |
| ≥3 | 1 (1.3%) | |
| Ultrasound before the 20 th week | 6 (7.9%) | |

Table 2. Adequacy of use of evidence-based interventions according to ANC (antenatal care) number of visits 4 to 7 (adequate ANC attendance)

| Screenings | ANC visits 4 to 7 (Adequate ANC) n=237 (46.4%) | |
|---|--|------------------------|
| First ANC attendance | >16 th week | <16 th week |
| | 46/202 (22.8%) | 156/202 (77.2%) |
| Blood group | 152 (64.1%) | |
| | 1 test | 2 tests |
| HIV | 104 (44.1%) | 126 (53.4%) |
| Syphilis | 212/235 (90.2%) | 2/235 (0.9%) |
| Hepatitis B | 143 (60.3%) | 0 |
| Malaria | 163 (68.8%) | 14 (5.9%) |
| Urine dipstick | 150 (63.3%) | 17 (7.2%) |
| Stool exam | 164 (69.2%) | 8 (3.4%) |
| Haemoglobin test | 158 (66%) | 25 (10.5%) |
| Timing of the haemoglobin test | < 20 th week | >20 th week |
| | 145 (61.2%) | 63 (26.6%) |
| Ultrasound | | |
| 0 | 92/236 (39.0%) | |
| 1 | 114 /236 (48.3%) | |
| 2 | 23/236 (9.7%) | |
| ≥3 | 7/236 (2.9%) | |
| Ultrasound before the 20 th week | 66 (27.8%) | |

Table 3. Adequacy of use of evidence-based interventions according to ANC (antenatal care) number of visits 8 or above (complete ANC attendance)

| Screenings | ANC visits 8 or above (Complete ANC) | |
|---|---|---------------------------------|
| | n=198 (38.7%) | |
| First ANC attendance | >16 th week | <16th week |
| | 13/189 (6.9%) | 176/189 (93.1%) |
| Blood group | 157 (79.3%) | |
| | 1 test | 2 tests |
| HIV | 57 (28.9%) | 129 (65.5%) |
| Syphilis | 179/197 (90.9%) | 4/197 (2.0%) |
| Hepatitis B | 120/196 (61.2%) | 1/196 (0.5%) |
| Malaria | 155 (11.1%) | 22 (11.1%) |
| Urine dipstick | 119 (60.1%) | 46 (23.2%) |
| Stool exam | 141 (71.2%) | 32 (16.2%) |
| Haemoglobin test | 114 (57.5%) | 63 (31.8%) |
| Timing of the haemoglobin test | < 20 th week | >20 th week |
| | 159 (80.3%) | 81 (40.9%) |
| Ultrasound | | |
| 0 | 57 (28.8%) | |
| 1 | 89 (44.9%) | |
| 2 | 47 (23.7%) | |
| ≥3 | 5 (2.5%) | |
| Ultrasound before the 20 th week | 89 (44.9%) | |

Discussion

A key component to reduce neonatal morbidity and mortality is having a high-quality ANC with a skilled provider [1, 2,3]. However, the neonatal mortality rate in Sao Tome and Principe remains high and it is necessary to unveil the proportion of women in STP obtaining complete ANC attendance with the essential interventions preconized. Therefore, with this study we aimed to know current ANC practices in the country, screenings performed, and antenatal problems commonly detected among pregnant women.

Regarding timing of first ANC visit and rate of attendance, we found that a high percentage (71.4%) of pregnant women attended before the 16th week. This finding is much higher compared to other studies in

sub-Saharan Africa, per example, Tanzania 12.4%, Nigeria with 15.4%, Zambia with 17%, and Ethiopia with 27.5% [7, 39, 40]. Practically all women had at least one visit, what is in accordance with the rate published by the UNICEF's 2019 Multiple Indicator Cluster Survey for Sao Tome and Principe (MICS6-STP) [27]. Complete ANC attendance (8 or above visits) was achieved by 38.7% of pregnant women and a total of 84% had the minimum of 4 visits. The uptake was found to be higher than reported for the country regarding a minimum of four visits (12.8%) and eight attendances (4.3%) [27]. It was also observed to be higher compared to the rates published for sub-Saharan countries with 13% of women not attending antenatal care at all and 53% having a minimum of 4 visits [41].

Detecting high-risk pregnancies is key in most prenatal programs in all developing countries and is also challenging [14]. Age and parity are the most frequently used risk factors to define high risk. Most evidence for using age and parity as risk criteria comes from studies of perinatal mortality but increased risk has also been demonstrated for women at the extremes of the fertile age range nulliparae or grand multiparae [42]. Women with risk factors for high-risk pregnancies have a one in four chance of developing complications than those with a low risk of high-risk pregnancies who have nearly one in ten [15, 42]. In this study, one third was registered as having a high-risk pregnancy in their antenatal cards, mainly due to advanced maternal age (16.8%) and teenage pregnancy (5.4%) as defined ≤ 16 years old in national guidelines. This is in accordance with the 10% to 30% rate reported worldwide of pregnancies estimated to be "at-risk" [15].

Regarding risky behaviours as alcohol consumption and the presence of domestic violence during pregnancy the percentage of notifications registered by the nurses in the antenatal cards was very low taking into consideration country MICS6-STP data [27]. One can speculate that healthcare providers are not motivated enough to ask and report these risks.

Height, weight, and body mass index are not registered during antenatal care visits in STP as it's not mandatory according to the WHO 2016 recommendations [13]. Details of previous pregnancies, contraception, planned pregnancy, present medical problems and signalling of high-risk pregnancies were often missing. The antenatal card should be designed to make documentation easier, but it was found that important information was not always adequately recorded. This may impact on both maternal and foetal outcomes [34].

Routine nutritional interventions and blood pressure measurement were met in a high proportion (80-85%) as recommended during antenatal period to prevent maternal anaemia, puerperal sepsis, low birth weight, and preterm birth [13].

Intermittent preventive treatment for malaria during pregnancy was provided to half of the women and a high proportion received an insecticide treated net, similar to other nearby countries as Gabon [43]. However, only 4.2% of pregnant women received a full IPTp-SP dose (at least two curative doses), a proportion much inferior compared to Gabon, that reaches 55% [43]. By contrast, bed net coverage was higher for STP (85.3%) than the estimated for Gabon (60%) [43].

Antenatal screening of HIV, hepatitis B virus and syphilis are free of charge and approximately all pregnant women (89 to 94%) had one test for HIV and syphilis done. Nevertheless, only half had two HIV tests and 1.2% tested twice for syphilis. When compared to other evidence-based screenings that have costs for women, this rate drops substantially. For instances, having two haemoglobin and urine tests is only accomplished by ten percent of those with adequate ANC (4-7 visits) and by thirty percent of those with complete ANC (8 or more contacts).

Regarding evidence-based interventions completion according to number of attendances, pregnant women with complete ANC had more two testes done for each screening in comparison to the pregnant women with adequate and inadequate ANC.

Around sixty percent of the pregnant women performed one obstetric ultrasound. Still, only half of them did it before the 20th-24th week. Missing an early ultrasound represents a lost opportunity for detection of multiple gestation, congenital anomalies, estimate gestational age, foetal malpresentation and placenta praevia and needs to be urgently addressed [14]. This reinforces that pregnancy costs are a blockage for reaching the optimal antenatal care.

Poverty may constitute a great barrier to accessing antenatal health services and can explain the incomplete use observed [41]. Pregnant women may not have the financial resources needed to pay for the services rendered, especially if they cost 17 USD when living on a budget of 1.40 USD per day. This may explain why a complete ANC utilization is reached only by 38.7% of pregnant women.

Then again, poverty alone doesn't explain why only half pregnant women are tested twice for HIV and only less than 2% for syphilis when these screenings are free. These findings also elucidate the existence of health system failures on the quality of ANC provision. As reported in other studies, offering total free ANC may be insufficient in improving ANC utilization because there are other significant barriers [54]. Understanding all the demographic, societal, and cultural factors such as economic status, residence, decision making, educational opportunities, and transportation could help improving women's health and accessibility to maternal health services [54].

Nonetheless, health system improvements that enhance the efficiency and broaden the benefits of free package for women reproductive health care services can go a long way to improve long term health gains for maternal and newborn health outcomes in Sao Tome and Principe.

Major gaps in the diagnosis, treatment and follow-up of pregnant women were identified through this study. For instance, anaemia during pregnancy is a public health problem that leads to different life-threatening complications and poor pregnancy outcomes [19]. In this study, 36.4% of pregnant women were anaemic and this finding is lower than official data from a previous study in the country that revealed an anaemia prevalence of 61% in pregnant women [29]. Illustrating a high rate of anaemia among pregnant women in STP when the overall prevalence for Africa is 41.82%, with differences between countries which ranged from 23.36% in Rwanda to 57.10% in Tanzania [19]. Thus, maternal

anaemia in STP should be urgently treated by national policy in order to enhance newborn health and survival [19].

Other maternal issue related to adverse neonatal outcomes identified in this study is the high prevalence of asymptomatic urinary tract infections in pregnancy. We identified a rate of 43.2% of asymptomatic bacteriuria (ASB), which is more than double of the range usually reported for pregnant women in LMIC (2% to 16.43%) [14]. Besides the high prevalence of ASB, we also identified that almost half of those in this situation go through all pregnancy without either receiving antibiotic treatment, neither repeating the urine tests. Furthermore, and unlike culture, strip urinalysis fails to identify the etiologic agents and the antibiotic sensitivity pattern. This practice will not allow proper management of urinary tract infection in pregnant women attending antenatal care in Sao Tome and Principe thus increasing their risk for complications. Additionally, the country doesn't have the resources to perform urine cultures. Due to the above reasons, the burden of urinary tract infections in pregnant women and its associated complications in this country is highly underestimated.

Intestinal infections by parasites are highly frequent in STP and in this study almost 55.5% of pregnant women had at least one parasite [47]. Anthelmintic treatment was administered in twenty percent of cases. Taking into account the country prevalence of anaemia, the implementation of preventive anthelmintic treatment for pregnant women, after the first trimester, as part of worm infection reduction programmes should be discussed [13].

HIV was detected in four (0.8%) pregnant women, what is in accordance with published data (0.2% in 2015) for the country [48]. Syphilis was diagnosed in five (1%) women and although the vast majority had done only one test, this percentage is much lower than the estimated pooled prevalence of syphilis (2.87%) in sub-Saharan Africa [18]. The STP's HIV and sexually transmitted infections programs led to a decrease in the incidence of syphilis in pregnant women and congenital syphilis. Syphilis in pregnant women significantly decreased from about 1.8% in 2008 to 0.8% in 2017 in the country [48]. There were no cases of congenital syphilis during that period. The percentage of women that required syphilis treatment in this study is identical to that published in other resourced-constrained countries as South Africa and Angola [34, 49]. This is a noteworthy point in the context of the triple elimination of HIV, syphilis and hepatitis B in Sao Tome and Principe. Regarding hepatitis B, expansion to universal newborn hepatitis B birth-dose vaccination (HepB-BD) without maternal screening started at the end of this study (third trimester of 2018) what is an excellent achievement for newborn health. Before that, the country had a selective hepatitis B birth-dose vaccination (HepB-BD) strategy targeting infants born to mothers who test positive for hepatitis B virus (HBV) surface antigen missing out many newborns as maternal screening for hepatitis B was low [50].

Typhoid fever is endemic in STP as common in low-resource environments that lack access to clean water and adequate sanitation [22]. Typhoid fever was registered for 14.8% pregnant women. However, the mean sensitivity, specificity, negative and positive predictive value of Widal test remains below 80% [44]. Therefore, the low specificity of this test and can lead to an over diagnosis of typhoid fever that may

result in the overuse of antibiotics and delay the proper treatment for underlying conditions [22]. The efficiency of Widal test in diagnosing typhoid fever without other confirmatory tests is not of diagnostic value, thus, it should not be recommended as a routine antenatal care practice in Sao Tome and Principe [44].

Gestational diabetes mellitus low rates in this study can also be underestimating the reality, taking into consideration, that half of the pregnant women only tested once and less than twenty percent tested twice throughout all pregnancy. Preeclampsia cases detected during ANC visits was of 7% what is in accordance to the range of 3% to 10% published for LMIC [51].

Another concern identified in this study is the risk for RhD alloimmunization as Rhesus factor was negative in 5.8% pregnant women. Similar frequency of RhD-negative phenotype was published in Nigeria 4.44%, 3.9% in Kenya, 4.06% in Guinea and 2.4% in Cameroon [25]. Although, it is a much lower than the $\geq 14\%$ prevalence of Rh-negative phenotype among Caucasians [25]. This risk of alloimmunization to RhD can cause perinatal adverse outcomes and compromise women's obstetric care in Sao Tome and Principe due to the unaffordability of anti-D immunoglobulin.

Sickle cell anaemia or the sickle cell trait was suspected in 13% pregnant women highlighting a crucial need to understand the burden of SCD in the country. Novel, rapid, inexpensive, and sensitive immunoassay-based point-of-care tests kits, found to have high sensitivity and specificity in sub-Saharan African settings should be available in STP for neonate screening programmes [24, 45, 46].

Sao Tome and Principe have made remarkable progress towards reaching a good coverage of ANC services and early attendance rates. Nevertheless, attending many antenatal care visits during pregnancy does not guarantee receiving the receipt of interventions that are effective in improving newborn health as highlighted in this study.

Conclusion

Sao Tome and Principe have made remarkable progress towards ensuring no pregnant woman is left without antenatal care. Nonetheless, most pregnant women still miss the opportunity to complete all evidence-based screenings. We supposed that this might contribute to the high rates of neonatal mortality reported for the country as the main ANC problems identified in this study were maternal anaemia and bacteriuria that are directly linked to adverse neonatal outcomes. Therefore, these should be urgently addressed to prevent newborn morbidity and mortality in the country. Additionally, attention is also needed for pregnant women with intestinal parasites infection, in risk of alloimmunization to RhD and with sickle cell anaemia. Strategies as 1) preventive administration of anthelmintic drugs after the first trimester, 2) implementation of universal access to anti-D immunoglobulin for the Rh-negative pregnant women and 3) providing novel inexpensive SCD point-of-care test kits in the country, should be discussed due to the country profile.

Regarding malaria control strategies, this study highlights that the use of full courses of IPTp-SP is still sub-optimal and insufficient and that efforts are still needed to achieve all pregnant women HIV and syphilis testing.

Quality ANC in the country is not yet ideal, partially due to the current partial free antenatal care health policy. Thus, a total free antenatal care is one public health measure that should be instigated in order to improve newborns' health outcomes. This study can, therefore, enlighten the government and stakeholders of the existence of ANC core obstacles in the country. It may also enable them to design effective interventions to reach the newborn health post-2015 Sustainable Development Goals of no more than 10 neonatal deaths per 1000 live births [52, 53].

Future studies

Understanding the determinants of pregnant women ANC utilization in Sao Tome and Principe and factors such as economic status, residence, decision making, educational opportunities can impact women's health and accessibility to maternal health services.

There are no previous studies in the country regarding the prevalence of bacteriuria among pregnant women and like many other LMIC, screening for bacteriuria is not always done routinely during antenatal care. Additionally, there is no knowledge about the burden, bacterial aetiology and, sensitivity pattern of maternal bacteriuria in the country. Further studies are needed to know the uropathogens and their sensitivity patterns in pregnant women attending antenatal care in STP.

The prevalence of sickle cell disease in Sao Tome and Principe is unknown and since the early diagnosis of the disease improves child survival, efforts should be made to study SCD burden in the country [24].

We also recommend further (qualitative) research into women's perceptions, and satisfaction with ANC and other maternity services as the research perceived a negative and fearful sensation regarding delivery at the main maternity as well reports of obstetric violence at the delivery time.

Strengths And Limitations

This study has the strength of being based on a large national sample. We included data from 518 antenatal cards from pregnant women similar to the recently published 2019 MICS6-STP from UNICEF [27]. Moreover, contrarily to MICS, our study is not vulnerable to recall bias as the mothers included had the antenatal card with them and had just delivered the baby.

However, there were some limitations that should be pointed: 1) being a retrospective study, the reasons for poorly recorded information were not explored, only the completeness of the recording could be analysed; 2) proper records and quality of care given could not be assessed; 3) this study was conducted in the capital city and may overestimate actual ANC visits as attitudes and practices may differ from those in rural areas in terms of access to health care, health worker motivation and training, and availability of health service.

Abbreviations

STP: Democratic Republic of Sao Tome and Principe; HAM: Hospital Ayres de Menezes; SDG: Sustainable Development Goal; ANC: antenatal care; DHS: Demographic and Health Survey; MICS: Multiple Indicator Cluster Survey; WHO: World Health Organization; LMIC: Low-to-Middle-Income Country; HIV: human immunodeficiency virus; ASB: asymptomatic bacteriuria.

Declarations

Ethics approval and consent to participate

Ethical clearance was obtained from the Democratic Republic of Sao Tome and Principe Ministry of Health and Hospital Ayres de Menezes. Written informed consent was obtained from all participants (or their parent or legal guardian in the case of adolescent under 16) after the purpose of the research was explained orally by the investigator.

This was done only after delivery to reduce coercion due to labour pains. Participation in the survey was voluntary as participants could decline to participate at any time during the study. All methods were performed in accordance with the relevant guidelines and regulations in practice.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

AV, MCM and FP carried out the conception and designing of the study. AV did all interviews and was responsible for data collection, performed statistical analysis and wrote the manuscript. MCM and FP critically evaluated and made progressive suggestions throughout the study and revising the manuscript.

MA and ALP performed statistical analysis and reviewed the manuscript. SS, NB and EC were involved in the study design at the country level. All the authors read and approved the final draft of the manuscript.

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References

1. Abou-Zahr CL, Wardlaw TM: Antenatal care in developing countries: promises, achievements, and missed opportunities: an analysis of trends, levels and differentials, 1990-2001 Geneva: WHO; 2003.
2. Mchenga M, Burger R, Von Fintel D. Examining the impact of WHO's Focused Antenatal Care policy on early access, underutilisation and quality of antenatal care services in Malawi: a retrospective study. *BMC health services research*. 2019 Dec;19(1):1-4.
3. Dowswell T, Carroli G, Duley L, Gates S, Gülmezoglu AM, Khan-Neelofur D, Piaggio G. Alternative versus standard packages of antenatal care for low-risk pregnancy. *Cochrane Database of Systematic Reviews* 2015, Issue 7. Art. No.: CD000934. DOI: 10.1002/14651858.CD000934.pub3.
4. Campbell OM, Graham WJ: Strategies for reducing maternal mortality: getting on with what works. *Lancet* 2006, 368:1284-1299.
5. World Health Organization. Making pregnancy safer: the critical role of the skilled attendant: a joint statement by WHO, ICM and FIGO: World Health Organization, Geneva; 2004.
6. World Health Organization. WHO recommendations on postnatal care of the mother and newborn: World Health Organization, Geneva; 2014.
7. Manyeh AK, Amu A, Williams J, Gyapong M. Factors associated with the timing of antenatal clinic attendance among first-time mothers in rural southern Ghana. *BMC pregnancy and childbirth*. 2020 Dec;20(1):1-7.
8. Ewunetie AA, Munea AM, Meselu BT, Simeneh MM, Meteku BT. DELAY on first antenatal care visit and its associated factors among pregnant women in public health facilities of Debre Markos town, North West Ethiopia. *BMC pregnancy and childbirth*. 2018 Dec;18(1):1-8.
9. Bloom SS, Lippeveld T, Wypij D. Does antenatal care make a difference to safe delivery? A study in urban Uttar Pradesh, India. *Health policy and planning*. 1999 Jan 1;14(1):38-48.
10. Ameyaw EK, Dickson KS, Adde KS. Are Ghanaian women meeting the WHO recommended maternal healthcare (MCH) utilisation? Evidence from a national survey. *BMC Pregnancy and Childbirth*. 2021

Dec;21(1):1-9.

11. Akowuah JA, Agyei-Baffour P, Awunyo-Vitor D. Determinants of antenatal healthcare utilisation by pregnant women in third trimester in peri-urban Ghana. *Journal of tropical medicine*. 2018 Feb 15;2018.
12. World Health Organization. *Mother-Baby Package: Implementing safe motherhood in countries. Practical Guide*. Document WHO/FHE/MSM/94.11. Geneva: World Health Organization 1994.
13. World Health Organization. *WHO Recommendations on Antenatal Care for a Positive Pregnancy Experience* [<https://apps.who.int/iris/bitstream/handle/10665/250796/9789241549912eng.pdf.jsessionid=FC8B1A05DB47E824E012407A5C1EB4A8?sequence=1>. Accessed 5 August 2021].
14. Crispín Milart, P.H., Prieto-Egido, I., Díaz Molina, C.A. et al. Detection of high-risk pregnancies in low-resource settings: a case study in Guatemala. *Reprod Health* 16, 80 (2019).
<https://doi.org/10.1186/s12978-019-0748-z>
15. Rajbanshi S, Norhayati MN, Nik Hazlina NH. High-risk pregnancies and their association with severe maternal morbidity in Nepal: A prospective cohort study. *PloS one*. 2020 Dec 28;15(12):e0244072.
16. World Health Organization. *WHO policy brief Dual HIV/Syphilis Rapid Diagnostic Tests can be used as the first test in antenatal care*. World Health Organization; 2019.
17. Awopegba OE, Kalu A, Ahinkorah BO, Seidu AA, Ajayi AI. Prenatal care coverage and correlates of HIV testing in sub-Saharan Africa: Insight from demographic and health surveys of 16 countries. *PloS one*. 2020 Nov 9;15(11):e0242001.
18. Hussen S, Tadesse BT. Prevalence of syphilis among pregnant women in sub-Saharan Africa: a systematic review and meta-analysis. *BioMed research international*. 2019 Jul 16;2019.
19. Liyew AM, Tesema GA, Alamneh TS, Worku MG, Teshale AB, Alem AZ, Tessema ZT, Yeshaw Y. Prevalence and determinants of anemia among pregnant women in East Africa; A multi-level analysis of recent Demographic and Health Surveys. *PloS one*. 2021 Apr 27;16(4):e0250560.
20. Farkash E, Weintraub AY, Sergienko R, Wiznitzer A, Zlotnik A, Sheiner E. Acute antepartum pyelonephritis in pregnancy: a critical analysis of risk factors and outcomes. *European journal of obstetrics, gynecology, and reproductive biology*. 2012 May; 162(1):24–7.
<https://doi.org/10.1016/j.ejogrb.2012.01.024> PMID: 22381037.
21. Oli AN, Okafor CI, Ibezim EC, Akujiobi CN, Onwunzo MC. The prevalence and bacteriology of asymptomatic bacteriuria among antenatal patients in Nnamdi Azikiwe University Teaching Hospital Nnewi; South Eastern Nigeria. *Nigerian journal of clinical practice*. 2010 Dec; 13(4):409–12. PMID: 21220855.
22. Mather RG, Hopkins H, Parry CM, et al. Redefining typhoid diagnosis: what would an improved test need to look like? *BMJ Global Health* 2019;4:e001831.
23. Kwala, K. H., & Asika, A. I. (2020). Prevalence of Typhoid Infection among Pregnant Women Attending Specialist Hospital Yola, Adamawa State, Nigeria. *Journal of Applied Life Sciences International*, 23(12), 93-101. <https://doi.org/10.9734/jalsi/2020/v23i1230210>

24. DeBaun MR, Galadanci NA (2019). Sickle cell disease in subSaharan Africa. Available at: <https://www.uptodate.com/contents/sickle-cell-disease-in-sub-saharan-africa> [Last accessed 2021 October 11].
25. Osaro E, Charles AT. Rh isoimmunization in Sub-Saharan Africa indicates need for universal access to anti-RhD immunoglobulin and effective management of D-negative pregnancies. *International journal of women's health*. 2010;2:429.
26. Knowles S, Poole G. Human blood group systems. In: Murphy MF, Pamphilon DH, editors. *Practical Transfusion Medicine*. 1st ed. London, UK: Blackwell Science; 2002. pp. 24–31.
27. INE e UNICEF. 2020. Inquérito de Indicadores Múltiplos 2019, Relatório final. Sao Tome , Sao Tome e Principe: Instituto Nacional de Estatística e Fundo das Nações Unidas para a Infância.
28. SÃO TOME AND PRINCIPE. Multiple Indicator Cluster Survey 2014 (MICS_2014). Final Report. National Institute of Statistics (INE), National Centre for Endemic Diseases (CNE), UNDP/ Global Fund Project, United Nations Childre´s Fund (UNICEF) and Government of the Democratic Republic of São Tome and Principe. São Tome and Principe, 2016. 444p.
29. República Democrática de Sao Tome e Principe Ministério da Saúde - Estratégia integrada de Saúde Reprodutiva, Materna, Neonatal, Infantil e do Adolescente e Nutrição 2019-2023_ Sao Tome , Setembro 2023files/pub-pdf/plano_sr_2019_2023.pdf
30. Tunçalp Ö, Pena-Rosas JP, Lawrie T, Bucagu M, Oladapo OT, Portela A, Metin Gülmezoglu A. WHO recommendations on antenatal care for a positive pregnancy experience—going beyond survival. *BJOG: An International Journal of Obstetrics & Gynaecology*. 2017 May;124(6):860-2.
31. VanDenHeuvel O, DeMey W, Buddingh H, Bots M. Use of maternal care in a rural area of Zimbabwe, a population-based study. *Acta obstetricia et gynecologica Scandinavica*. 1999 Jan 1;78(10):838-46.
32. Simkhada B, Teijlingen ER, Porter M, Simkhada P. Factors affecting the utilization of antenatal care in developing countries: systematic review of the literature. *Journal of advanced nursing*. 2008 Feb;61(3):244-60.
33. Giovanni Zanconato; Regina Msolomba; Laura Guarenti; Massimo Franchi (2006). Antenatal care in developing countries: The need for a tailored model. , 11(1), 15–20. doi:10.1016/j.siny.2005.10.002
34. Ibe-Dladla NS, Adam Y. Audit of the patient-carried antenatal card, South Africa. *African Journal of Midwifery and Women's Health*. 2018 Oct 2;12(4):168-72.
35. World Health Organization. WHO antenatal care randomized trial: manual for the implementation of the new model, WHO document WHO/RHR/01.30. Geneva: WHO; 2002.
36. Parry CM, Wijedoru L, Arjyal A, et al. The utility of diagnostic tests for enteric fever in endemic locations. *Expert Rev Anti Infect Ther* 2011;9:711–25.doi:10.1586/eri.11.47
37. Adekile A, Anie KA, Ben Hamda C, et al. The Sickle Cell Disease Ontology: enabling universal sickle cell-based knowledge representation. *Database (Oxford)* 2019; 2019: 1–12.
38. Schneider RG, Alperin JB, Lehmann H. Sickling tests: Pitfalls in performance and interpretation. *JAMA*. 1967 Oct 30;202(5):419-21.

39. Gebresilassie, B., Belete, T., Tilahun, W. et al. Timing of first antenatal care attendance and associated factors among pregnant women in public health institutions of Axum town, Tigray, Ethiopia, 2017: a mixed design study. *BMC Pregnancy Childbirth* 19, 340 (2019). <https://doi.org/10.1186/s12884-019-2490-5>
40. Gebremeskel F, Dibaba Y, Admassu B. Timing of first antenatal care attendance and associated factors among pregnant women in Arba Minch Town and Arba Minch District, Gamo Gofa Zone, South Ethiopia. *Journal of environmental and public health*. 2015 Oct 12;2015.
41. Adedokun ST, Yaya S. Correlates of antenatal care utilization among women of reproductive age in sub-Saharan Africa: evidence from multinomial analysis of demographic and health surveys (2010–2018) from 31 countries. *Archives of Public Health*. 2020 Dec;78(1):1-0
42. Høj L, Da Silva D, Hedegaard K, Sandström A, Aaby P. Factors associated with maternal mortality in rural Guinea-Bissau. A longitudinal population-based study. *BJOG: an international journal of obstetrics and gynaecology*. 2002 Jul 1;109(7):792-9.
43. Bouyou-Akotet MK, Mawili-Mboumba DP, Kombila M. Antenatal care visit attendance, intermittent preventive treatment and bed net use during pregnancy in Gabon. *BMC Pregnancy and Childbirth*. 2013 Dec;13(1):1-6.
44. Mengist HM, Tilahun K. Diagnostic value of Widal test in the diagnosis of typhoid fever: a systematic review. *J Med Microbiol Diagn*. 2017;6:248.
45. Makani J, Moshi G. Haematology in sub-Saharan Africa: advances and opportunities in health care, education, and research. *The Lancet Haematology*. 2021 Oct 1;8(10):e678-81.
46. Esoh K, Wonkam-Tingang E, Wonkam A. Sick cell disease in sub-Saharan Africa: transferable strategies for prevention and care. *The Lancet Haematology*. 2021 Sep 2.
47. Ferreira FS, Baptista-Fernandes T, Oliveira D, Rodrigues R, Neves E, Lima A, Garrido E, Afonso G, Zaky A, Telles de Freitas P, Atouguia J. *Giardia duodenalis* and soil-transmitted helminths infections in children in Sao Tome and Principe: do we think *Giardia* when addressing parasite control?. *Journal of tropical pediatrics*. 2015 Apr 1;61(2):106-12.
48. Ministério da Saúde_ República Democrática de Sao Tome e Principe_Plano Nacional do Desenvolvimento da Saúde 2017-2021
49. Oliveira D, do Rosário Martins M, Castro R, Cordeiro L, Barroso MR, Nazaré MA, Pereira F. HIV, HBV and syphilis screening in antenatal care in Lubango, Angola. *Sexually transmitted infections*. 2020 Dec 1;96(8):621-2.
50. Hagan JE, Carvalho E, Souza V, Queresma Dos Anjos M, Abimbola TO, Pallas SW, Tevi Benissan MC, Shendale S, Hennessey K, Patel MK. Selective Hepatitis B Birth-Dose Vaccination in Sao Tome and Principe: A Program Assessment and Cost-Effectiveness Study. *Am J Trop Med Hyg*. 2019 Oct;101(4):891-898. doi: 10.4269/ajtmh.18-0926. PMID: 31392947; PMCID: PMC6779202.
51. Hounkpatin, O.I., Amidou, S.A., Houehanou, Y.C. et al. Systematic review of observational studies of the impact of cardiovascular risk factors on preeclampsia in sub-saharan Africa. *BMC Pregnancy Childbirth* 21, 97 (2021). <https://doi.org/10.1186/s12884-021-03566-2>

- 52. Lawn JE, Blencowe H, Oza S, You D, Lee ACC, Waiswa P, et al. Every newborn: Progress, priorities, and potential beyond survival. *Lancet*. 2014;384(9938):189–205.
- 53. Switow M. Post 2015–What Comes After the Millennium Development Goals. *Social Space*. 2013:94-102.
- 54. Adeniyi Francis Fagbamigbe & Erhabor Sunday Idemudia (2017) Wealth and antenatal care utilization in Nigeria: Policy implications, *Health Care for Women International*, 38:1, 17-37, DOI: 10.1080/07399332.2016.1225743

Figures

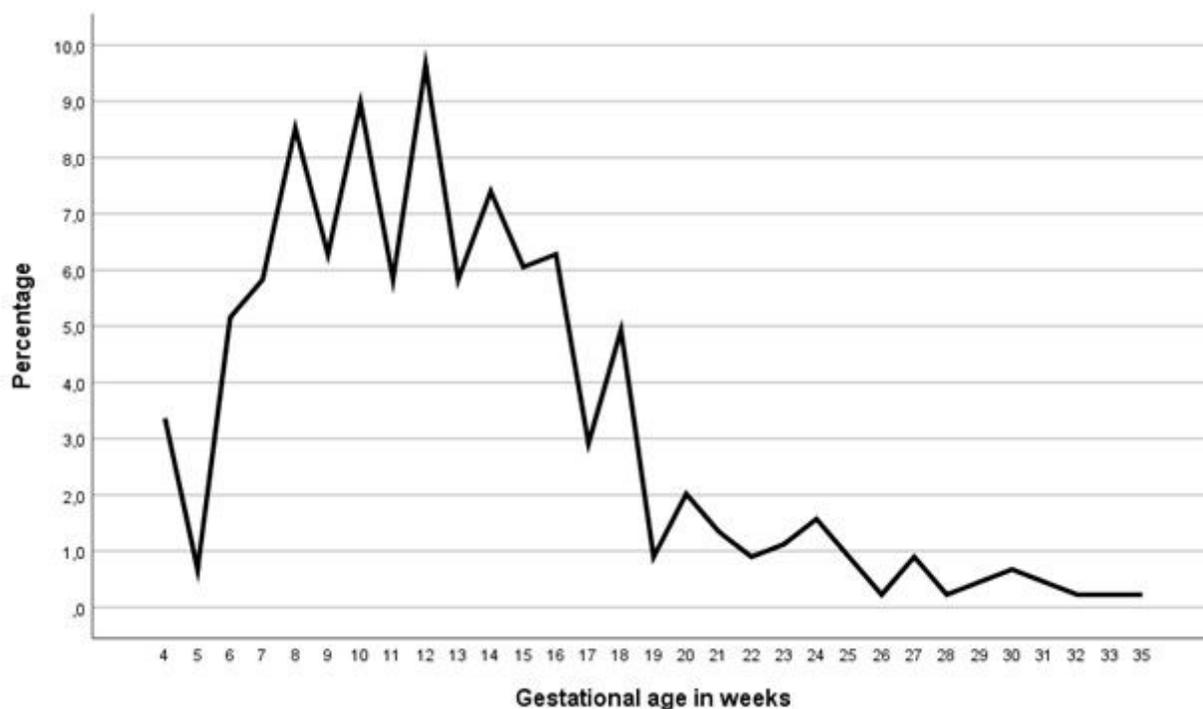


Figure 1

Percentage of pregnant women by gestational age in weeks during first attendance at antenatal care facility