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Antenatal Deworming and Materno-Perinatal Outcomes in Calabar, Nigeria

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Abstract

BACKGROUND: Studies have shown that administration of anthelmintic drugs in pregnancy can reduce the incidence of maternal anaemia; however, data on other maternal and perinatal outcomes are limited.

AIM: This study was therefore conducted to evaluate the direct impact of mass deworming on delivery and perinatal outcome.

MATERIAL AND METHODS: A total of 560 healthy pregnant women in their second trimester were randomised to receive a single dose of oral mebendazole (500 mg) and placebo. Each participant received the standard dose of iron supplement and malaria prophylaxis. They were followed up to delivery and immediate postpartum period to document the possible impact on maternal and perinatal outcomes.

RESULTS: The prevalence of anaemia at term, 37 weeks gestation and above, among the treatment arm was 12.6% compared with 29.9% in the placebo arm ($p < 0.001$). Caesarean section rates was higher in the treated group and the placebo ($p = 0.047$).There were no statistically significant differences in incidences of postpartum haemorrhage ($p = 0.119$), Puerperal, pyrexia ($p = 0.943$), low birth weight ($p = 0.556$) asphyxia ($p = 0.706$) and perinatal death ($p = 0.621$).

CONCLUSION: Presumptive deworming during the antenatal period can significantly reduce the incidence of peripartum anaemia. However, more studies may be needed to prove any positive perinatal outcome.

Introduction

Intestinal parasitic infections are of public health importance because of likely morbidity related to iron deficiency anaemia due to chronic blood loss suffered by the hosts [1]. The burden is much for children and pregnant women because of the increased requirement for iron and other nutrients [2]. About two decades ago, a study in the general population in Calabar by Ejezie GC and Akpan IF [3] showed a high prevalence of intestinal nematodes of 28.5% and recently, 23.6% prevalence has been reported by Ozumba UC et al., [4] among pregnant women at a University Teaching Hospital, in Southern Nigeria. However, these studies did not assess the correlation with anaemia among the subjects which necessitates more prospective studies to determine the impact of this high helminths prevalence on the haematological status and pregnancy outcome in the pregnant populace.

It has been reported that majority of the pregnant women in the tropics have depleted or borderline iron stores due to menstrual blood loss and the demands of previous pregnancies, and only a few women in low-income countries begin pregnancy with sufficient iron stores [5] [6] [7] [8]. Combined with the increased iron demands in pregnancy due to the expansion in red cell mass and the requirement of the developing foetus, many women become iron deficient during childbearing [4]. The prevalence of iron deficiency anaemia in pregnancy is quoted at 56% in developing countries [7]. Hence, parasitic diseases particularly soil-transmitted intestinal helminthic infections are important public health problems confronting many women in the developing countries [6] [8].

Furthermore, it is estimated that anaemia may be responsible for as much as 20% of all maternal deaths in sub-Saharan Africa through three main mechanisms [9]: Firstly, anaemia makes women more susceptible to deaths from haemorrhage by lowering their haemoglobin reserves for blood loss especially at birth. Severe anaemia is associated with increased susceptibility to infection due to lowered resistance to disease, and haemoglobin level of less than 4 g/dl is associated with high-risk cardiac failure, particularly during delivery or in the immediate post-partum period, making the women likely to die if not properly managed [9].

Although it is widely believed that deworming can improve anaemic status in pregnant women [10] [11] little information is available about the degree to which anaemia improves after deworming in Calabar and improvement in the pregnancy outcome. Hence, it is necessary to conduct this randomised controlled study to suggest effective evidence-based methods of controlling anaemia and improving maternal health. And despite WHO recommendation of a single dose of Albendazole or Mebendazole treatment after the first trimester for infected pregnant women and mass policy (presumptive treatment) in areas where the infection is endemic (prevalence>20-30%) and where anaemia is highly prevalent, [12] it is yet to be included in routine antenatal care package in the University of Calabar Teaching Hospital, Calabar and many other tertiary health institutions in Nigeria. Low birth weight due to maternal chronic anaemia is a major factor influencing neonatal and infant survival. So treatment of helminthiasis in pregnancy may be beneficial to maintain appropriate fetal weight [12] [13]. Anthelminthics alone may halt the iron loss, or reduce the rate of loss, and the addition of iron supplements is likely to improve the haemoglobin or packed cell volume (PCV) levels.

This study was therefore conducted to evaluate the direct impact of mass deworming on delivery and perinatal outcome.

Material and Methods

The research was conducted at the University of Calabar Teaching Hospital Antenatal Clinic from 1st January to 31st December 2015. The hospital is the only tertiary health facility in Calabar Metropolis, the capital of Cross River State which is located in South-South Zone of Nigeria. A review of antenatal records revealed that the hospital provides obstetrics services to between 1500 and 2200 pregnant women annually. The hospital practices routine antenatal care schedules, i.e. four weekly visits for the 1st 28 weeks after that 2 weekly till 36 weeks, then weekly till delivery. The study population comprised all consenting women attending antenatal care at the University of Calabar teaching hospital who meet the criteria during the study period.

Of the 560 participants in this study, 300 received mebendazole while 260 made up the placebo arm. A sample size of 300 was adopted for the treatment arm using Leslie Kish formulae. The actual calculated sample size was 280 but to cater for attrition or “drop out” 300 women were recruited into the treatment arm. The sample size was determined using 23.6% prevalence from a recent study among pregnant women with precision at 0.05 and 95% confidence interval.

Women who presented for antenatal care at the University of Calabar teaching hospital were recruited in their second trimester during the study period. The research and its purpose and expected benefits to the patients and the community were explained, and consent was obtained from the willing participants. To facilitate easy completion of questionnaires, semi-structured and closed-ended questions were used. Consenting women were assured of confidentiality. They were informed that no money would be charged for the test performed or for the anthelminthic/placebo drugs.

This was a randomised placebo-controlled study. The study consisted of two groups of pregnant women, the treatment and the placebo group. The study design was suitable for this particular research because the placebo group constituted the baseline of what can be assumed to be expected the outcome in normal circumstances without treatment. The participants were assessed for eligibility using the inclusion and exclusion criteria below. The women were then randomised to receive either a single 500 mg oral dose of Mebendazole plus a daily iron supplement, (60 mg elemental iron) and folic acid or a single dose placebo plus a daily iron supplement (60 mg elemental iron) and folic acid. The administration of the anthelmintics was done by directly observed therapy (DOT) to ensure 100% compliance. Computer-generated random numbers were used for sampling. Single tablet (500 mg) of mebendazole was wrapped in a paper and labelled with a number for identification from the placebo which was also wrapped with same paper to blind the patients and the dispenser. Presumptive treatment was adopted in this study due to ethical issues in leaving some women with proven infections from stool microscopy untreated. All the participants received intermittent preventive treatment for malaria (IPT) according to the National protocol. The baseline packed cell volume (PCV) was noted at recruitment. All the participants in both the treatment and the placebo groups were then followed up to term and delivery. The maternal and perinatal outcomes were documented. Outcomes of interest included the prevalence of peripartum anaemia (PCV < 33%), mode of delivery post-partum haemorrhage, and other maternal morbidity like puerperal pyrexia; perinatal outcome included the

proportion of low birth weight, birth asphyxia, congenital abnormally and perinatal mortality.

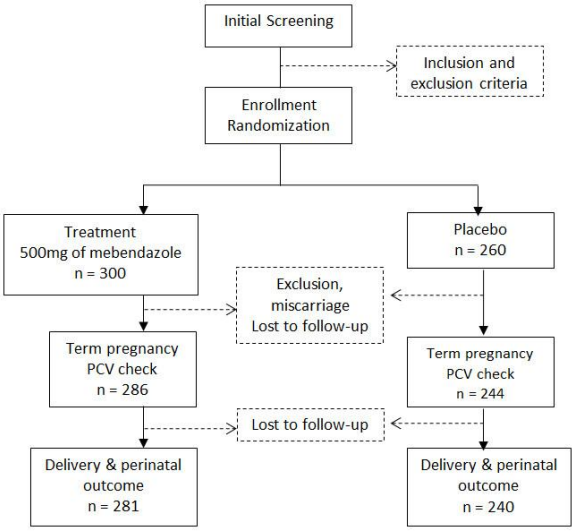

Figure 1: Summary of the study design (Flow diagram)

Data were collected using pre-tested interviewer-administered questionnaire which contains socio-demographic characteristics (age, educational qualification, occupation, the occupation of spouse marital status, place of resident) obstetric and gynaecological history; drug history (haematinics, antimalarial, anthelminthics) and previous drug reaction or allergy; past and present medical and surgical history.

Data were analysed using SPSS version 19. Description of means, frequency, proportions and rates of given data for each variable was calculated. Bivariate analysis was done to see the association of each independent variable with the outcome variable. A multivariate logistic regression model was used to identify the effect of each independent variable with the outcome variable. A p value of less than 0.05 was considered statistically significant.

Inclusion criteria: 1) consenting women; 2) gestational age from 14 weeks to 28 weeks by LMP or ultrasound, and 3) singleton pregnancy.

Exclusion criteria: 1) history of vaginal bleeding in current pregnancy; 2) medical, surgical or obstetric complication; 3) diagnosed or suspected multiple pregnancies; 4) patients with haemoglobinopathy; 5) women with moderate to severe anaemia; and 6) allergy to Mebendazole or sulphadoxine.

Formal approval was obtained from the research ethics committee of the University of Calabar Teaching Hospital before the research was commenced. Written informed consent was obtained from each study participant after they were introduced to the purpose of the study and informed about their right to interrupt the researcher or withdraw at any time. Women who were detected to be anaemic were given appropriate treatment. Confidentiality was maintained at all levels of the research.

The research assistants were trained in history taking, physical examination and data recording. They were trained on filling the questionnaire in a standard way. Haematological tests were done in the same laboratory. The laboratory internal and external quality control measures were adhered to. A haematologist reviewed the haemograms. There was a meticulous recording of laboratory investigation results. The same haematinic was given to all the participants. To avoid contamination of placebo group with the treatment arm, each participant's folder was identified with a number on a sticker which helped the investigator to differentiate them. This was also used to follow-up the women to term and delivery. The sticker was removed at the time of discharge from the hospital before the folder was sent to health record department for filing.

Results

Out of the 300 women recruited into the treatment arm, 281 (93.7%) of them continued till delivery giving a drop-out rate of 6.33%. The mean age of respondents in both groups was similar; 29.3 ± 4.4 years for the study group and 29.7 ± 4.6 years for the control group (p = 0.062). Table 1 summarises the socio-demographic characteristics of respondents.

Table 1: Socio-demographic characteristics of respondents by group

Variable	Study N = 286 Freq (%)	Control N = 244 Freq (%)	Total N = 530 Freq (%)	X2	P-value
Age (years)					
< 20	4 (1.4)	1 (0.9)	5(0.9)	Fisher's Exact	0.062
20-29	136 (47.6)	118 (48.4)	254 (47.9)		
30-39	146 (51.0)	120 (49.2)	266 (50.2)		
≥ 40	0 (0.0)	5 (2.0)	5 (0.9)		
Mean ±SD	29.3 ± 4.4	29.7 ± 4.6	29.5 ± 4.5		
Residence					
Urban	276 (96.5)	234 (95.9)	510 (96.2)		
Rural	10 (3.4)	20 (3.8)	10 (4.1)	Fisher's Exact	0.825
Parity					
0	96 (33.6)	49 (20.1)	145 (27.4)		
1-4	187 (65.4)	187 (76.6)	374 (70.6)	14.269	0.001*
> 4	3 (1.0)	8 (3.3)	11 (2.1)		

A higher proportion of participants in the control group (29.9%) compared with the study group (12.6%) had anaemia at term. The PCV difference of respondents in the study and control groups was assessed. Participants with a positive difference were more (57.0%) in the Mebendazole group compared with (29.9%) in the placebo group. Those with either no difference or negative difference were more (22% and 61.1% respectively) in the control group compared with the study group (6.3% and 36.7%

respectively). These differences were statistically significant (p < 0.001). In the mebendazole group, 64.3% of the anaemic women had mild anaemia (Hb = 10 to 10.9 g/dl) while the remaining (35%) had moderate anaemia (7 to 9.9 g/dl). There was no incidence of severe anaemia in the treatment arm (Hb < 7.0 g/dl). One case of severe anaemia was noted in the placebo group while 79.2% and 19.4% of the reported anaemia in this group was mild and moderate respectively.

Table 2 shows multivariate logistic regression analysis of factors associated with anaemia among study respondents. Only parity (OR = 5.063, 95% CI = 1.531-16.743) was found to be an independent predictor of anaemia among the study group. Those with parity above 3 were significantly more likely to have anaemia at term.

Table 2: Determinants of anaemia among respondents in the study group

Characteristic	Odds Ratio	95% Confidence interval	P-value
Age			
≤29	1.815	0.816-4.039	0.144
>29	1		
Parity >3	5.063	1.531-16.743	0.008
Yes	1		
No	5.063		
Social class			
1 to 2		0.324-1.485	0.346
3 to 5	1		
Gestational age at term			
<24	0.829	0.396-1.736	0.618
>24	1		
Residence			
Urban	1.091	0.128-9.291	0.937
Rural	1		

Table 3 below shows the birth weight group of respondents' babies. Majority of respondents had babies with normal birth weight 455 (85.8%). This was slightly higher among study group 248 (86.7%) compared with control group 207 (84.4%). Overall, 40 (7.5%) had babies with higher than normal birth weight, 4 kg and above, slightly higher in the study group 23 (8.0%) compared with control group 17 (7.0%) while 20 (3.8%) had low birth weight babies, slightly lower in study group 9 (3.1%) compared with control group 11 (4.5%). These differences were not statistically significant (p = 0.556). The overall mean birth weight of babies was 3.23 ± 0.629 kg; 3.26 ± 0.582 kg in the study group and 3.19 ± 0.679

Table 3: Birth weight group of respondents' babies by study arm

Variable Birth weight group/Kg (%)	Study group	Control group	Total	$\chi 2$	P-value
ELBW (<1.0)	6 (2.1)	9 (3.7)	15 (2.8)	2.079	0.556
VLBW (1-1.4)	0 (0.0)	0 (0.0)	0 (0.0)		
LBW (1.5-2.4)	9 (3.1)	11 (4.5)	0 (3.8)		
Normal (2.5-3.9)	248 (86.7)	207 (84.8)	455 (85.8)		
Macrosomia (≥4)	23 (8.0)	17 (7.0)	40 (7.5)		
Mean birth weight ± SD	3.23 ± 0.629	3.19 ± 0.679	3.26 ± 0.582		

Most of the participants, 94.7% in the study group and 95.1% in the controlled group, did not experience postpartum haemorrhage (PPH) while 4.2% in the study group and 4.9% in the control group had PPH. The slight differences were not statistically significant (p = 0.119). Also, incidences of puerperal pyrexia were compared. Almost equal percentage in both study (94.8%) and control (94.3%) had no incidence of puerperal pyrexia, and almost equal proportion had pyrexia; 3.5% in the study group and 3.7% in control group. There was no statistically significant difference in pyrexia by study arm (p = 0.943).

The perinatal deaths were: 2.9% in (29 per 1000) study group and 3.3% (33 per 1000) in control group (Fig. 2).

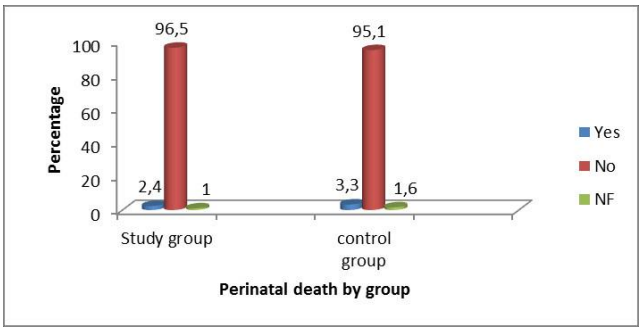

Figure 2: Perinatal death by a group

Only two babies, one from each group, were born with a gross congenital anomaly. Furthermore, the incidences of birth asphyxia were comparable. The study shows the percentage of participants whose babies had asphyxia (5.6% in the study group and 7.05% in control group) and had no asphyxia (93.4% in the study group and 95.1% in control group). The slight difference in this experience was not significant statistically (p = 0.706). Table 3 summarises proportion of normal birth weight (2.5-3.9 kg), low birth weight (LBW), very low birth weight (VLBW) and extremely low birth weight (ELBW).

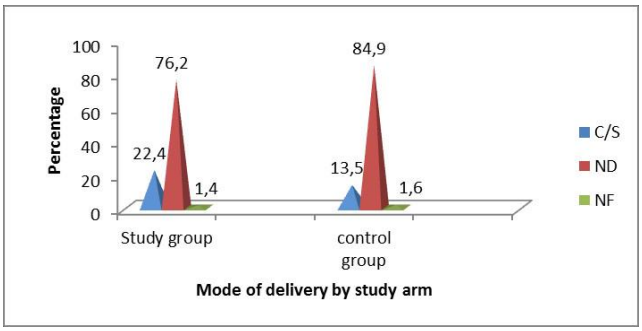

Figure 3: Mode of delivery by study arm (p = 0.047); C/s = caesarean section; ND = Normal delivery; NF = Lost to follow up

The study shows that more women who received mebendazole were delivered by caesarean section. Fig. 3 below shows the mode of delivery of participants by study arm. The majority of both study and control had normal delivery; 76.7% in the study group and 84.9% in control group. In the study group, 22.4% delivered by C/S compared with 13.5% in the control group.

Discussion

The drop-out rate of 6.33% in this study was similar to 7% obtained in a previous randomised trial in Uganda [14]. As every participant was dully counselled on the need for continued care at the centre, the drop-out could have been due to miscarriages, change of place of residents/relocation or other factors. The prevalence of anaemia at term (after treatment) in the study group was 12.6% and was significantly lower than the prevalence of 29.9% among the control/ placebo arm (p=0.000l). This statistically significant difference is the evidence of the negative effect of helminth infection on maternal haemoglobin concentration with associated impact on overall maternal health. Perhaps the elimination of intestinal parasites has significantly contributed to the reduction in the incidence of anaemia at term among the treated women. Several studies have found a strong association between anaemia and intestinal parasitic infestations [4] [15] [16] [17] [18].

In controlling for the co-founders or other related risk factors for anaemia using multiple logistic regression, the study shows that high parity was an independent risk factor for anaemia at term among the participants. The women with more than three previous pregnancies had significantly higher rates of anaemia. This is in keeping with findings from other studies especially in Africa and Latin America [19]. Also, a study in south India [20] reported a higher incidence of anaemia for the parity index more than four. This might be due to the increase in women's nutritional needs during pregnancy in the setting of low iron store especially due to short inter-pregnancy intervals. This further highlights the role of contraceptives in improving maternal health.

The observed higher caesarean section rate among the treatment group might have been contributed by the relative increase in the incidence of macrosomic births (birth weight > 4.0 kg) among other indications. However, the study failed to show any significant statistical difference in the incidence of postpartum haemorrhage (p = 0.119), and puerperal pyrexia (p = 0.943) between the treatment and the placebo arms. Improved maternal care in the facility may have significantly reduced the risk of these morbidities since the study was conducted in a tertiary health centre with the availability of specialised care. The association between maternal anaemia and increased risk of postpartum haemorrhage has been reported. Significant anaemia may cause postpartum haemorrhage by impairing myometrial contraction (atony) following delivery [21]. Similarly, puerperal sepsis has been linked to peripartum anaemia [22]. In this study, most of the anaemic women had mild anaemia probably because of iron supplementation they received during pregnancy, and this might have influenced the low incidence of postpartum haemorrhage among the participants.

In this study, although there was a remarkable improvement in the haematologic status of women treated with the anthelminthic drug in pregnancy, these did not significantly translate to improvement in fetal or neonatal well-being. The research showed a slightly higher mean birth weight in the study (3.26 ± 0.582 kg) than the placebo group (3.19 ± 0.679). There was no statistically significant difference in low birth weight (p = 0.556). The incidence of very low birth weight and extremely low birth weight were very rare in this study. Also, there was no significant difference in perinatal death (p = 0.621) and birth asphyxia (p = 0.706). Two congenital abnormal infants were delivered, one in each group. Similar findings were documented in previous studies [28] [29]. Furthermore, several other studies on helminths infection and anaemia on pregnancy outcomes have yielded inconsistent results [30] [31] [32] [33] [34] [35] [36] [37] [38] [39] [40] [41] [42]. For instance, these findings in this study contrast with 2 previous observational studies [41] [42] in which women who received mebendazole or albendazole were compared with those who did not. One possible mechanism for a beneficial effect on birth weight would be through increased maternal haemoglobin level, and an effect of anthelminthics on perinatal mortality might be mediated by improved birth weight. It is possible that women in those other studies cited who missed one or both doses of albendazole may also have missed their haematinics doses. Similarly, the findings of a cross-sectional study in Sierra Leone [42] in which a lower rate of perinatal deaths occurred among women who took mebendazole may have been affected by selection bias and unmeasured confounders due to lack of randomisation.

In our study since every participant received the standard dose of iron supplement in addition to malaria control strategy (IPT and LLIN) which possibly resulted in the overall decline in the prevalence of anaemia in both arms with very few of them having moderate to severe anaemia, the incidence of low birth weight was low. This must have impacted positively on the perinatal outcome in both groups. Low birth weight has been associated with other perinatal complications including birth asphyxia and perinatal death [34] [42]. Furthermore, deworming is important to prevent some direct pathological effects of worms on the newborn. This is because helminths infection has been linked to the long-term effect on the development of the foetal immune system and risks for disease susceptibility in later life [34].

In conclusion, mass deworming in pregnancy is effective in reducing the incidence of anaemia in advanced gestation. However mild to moderate anaemia may not significantly impact negatively on the perinatal outcomes. The same may not, however, apply to women who are not on routine iron and folic acid supplement during pregnancy as severe anaemia may worsen life-threatening obstetric complications and infant health. There is need to consider 2nd-

trimester presumptive treatment for inclusion in our routine antenatal care practice.

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References

1. Crompton DWT. The Public Health importance of Hookworm disease. Parasitol. 2000; 121:S39-S50. https://doi.org/10.1017/S0031182000006454

2. Prevention and Control of Schistosomiasis and Soil-transmitted Helminthiasis. Report of WHO Expert Committee, Geneva, 2002.

3. Glover-Amengor M, Owusu WB, and Akanmor BD. Determinants of Anaemia in Pregnancy in Sekyere West District, Ghana. Ghana Med J. 2005; 39(3):102-107. PMid:17299553 PMCid:PMC1790823

4. Ozutnba DC, Ozumba NA and Anya Samuel. Helminthiasis in Pregnancy in Enugu, Nigeria. Journal of Health Science. 2005; 51(3): 291-293. https://doi.org/10.1248/jhs.51.291

5. Ndibazza J, Muhangi L, Akishuce D, Kiggundu M, Ameka C, Omeka J et al. Effect of Deworming during Pregnancy on Maternal and Perinatal Outcomes in Entebe, Uganda: A Randomized Controlled Trial Clinical Infectious Diseases. 2010; 50: 531-40. https://doi.org/10.1086/649924 PMid:20067426 PMCid:PMC2857962

6. World Health Organization (WHO). Report of the WHO informal consultation on Hookworm Infection and Anaemia in Girls and Women, 1994. Geneva, Switzerland, WHO, 1994.

7. Kalaivani K. Prevalence and Consequences of Anaemia in Pregnancy. Indian J Med Res. 2009; 130: 627-633. PMid:20090119

8. Strong J. Haematinics deficiencies. In: The Obstetric haematology manual (Sue P & Hint B edn). Cambridge University Press, 2010; 2:13-27.

9. Letsky EA. Erythropoiesis in pregnancy. J Perinat Med. 1995; 23:39-45. https://doi.org/10.1515/jpme.1995.23.1-2.39 PMid:7658318

10. Buseri FI, Uko EK, Jerimiah ZA, Usanga EA. Prevalence and Risk Factors of Anaemia among Pregnant women in Nigeria. The Open Haematology Journal. 2008; 2:14-19. https://doi.org/10.2174/1874276900802010014

11. Damen JG, Banwat EB, Egah DZ, Allanana JA. Parasitic contamination of vegetables in Jos, Nigeria. Ann Afr Med. 2007; 6(3):115. https://doi.org/10.4103/1596-3519.55723 PMid:18240499

12. Damen JG, Luka3, Biwan El, LugosM. Prevalence of Intestinal Parasites among pupils in ruraTNorth Eastern Nigeria, Nigeria. Niger Med J. 2011; 52:4-6. PMid:21969128 PMCid:PMC3180756

13. Ejezie GC, Akpan IF. Human Ecology and parasitic infections. The effect of occupation on the prevalence of parasitic infection in Calabar, Nigeria. Journal of Hygiene, Epidemiology, Microbiology and Immunology.1992; 36(2):161-165. PMid:1512451

14. World Bank. World Development Report 1993: Investing in Health. New York, Oxford University Press, 1993.

15. World Health Report 1999. Making a Difference. Geneva, World Health Organization, 1999.

16. Pawlowski ZS, Schad GA, Stott GJ. Hookworm Infection and Anaemia. Geneva, World Heaht Organization, 1991.

17. Sharma JB. Nutritional Anaemia during Pregnancy in non-industrialized countries. Progress in Obstetrics and Gynaecology. 2003; 15(7):103-124.

18. Torlesse H, Hodges M. Anthelminthic treatment and haemoglobin concentrations during pregnancy. Lancet. 2000; 356:1083. https://doi.org/10.1016/S0140-6736(00)02738-0

19. Christian P, Khatry SK, West KP. Antenatal Anthelminthic Treatment, Birth weight and Infant Survival in Rural Nepal. Lancet. 2004; 364:981-3. https://doi.org/10.1016/S0140-6736(04)17023-2

20. Report of the WHO Informal Consultation on the use of Chemotherapy for the Control of Morbidity due to Soil-transmitted Nematodes in Humans, Geneva, 29 April to 1 may 1996. Geneva, World Health Organization (document WHO/CTD/SIP/96.2), 1996.

21. The Use of Essential Drugs. Ninth Report of the WHO Expert Committee (including the revised Model List of Essential Drugs). Geneva, World Health Organization (WHO Technical Report Series, No. 895), 2000.

22. Liabsuetrakul T. Epidemiology and the Effect of Treatment of Soil-transmitted Helminthiasis in Pregnant Women in Southern Thailand. Southeast Asian J Trop Ned. 2009; 2(40): 211-222.

23. Ladva S. Effect of Administration of Anthelminthics for Soil-transmitted Helminths during Pregnancy. Cochrane Library, 2009.

24. Report of the WHO Informal Consultation on Monitoring of Drug Efficacy in the Control of Schistosomiasis and Intestinal Nematodes, Geneva, 8-10 July 1998. Geneva, World Health Organization (document WHO/CDS/SIP/99.1), 1999.

25. Diav-Citrin et al. Pregnancy Outcome after Gestational Exposure to Mebendazole: A Prospective Controlled Cohort Study. American Journal of Obstetrics and Gynaecology. 2003; 188:282-285. https://doi.org/10.1067/mob.2003.79

26. De Silva NR, et al. Effect of Mebendazole Therapy in Pregnancy on birth outcome. Lancet. 1999; 353:1145-1149. https://doi.org/10.1016/S0140-6736(98)06308-9

27. ACS N, et al. Population-based Case-control Study of Mebendazole in Pregnant Women for Birth Outcomes. Congenital Anomalies. 2005; 45: 85-88. https://doi.org/10.1111/j.1741-4520.2005.00072.x PMid:16131365

28. Gyorkos TW, Larocque R, Casapia M, Gotuzzo E. Lack of Risk of Adverse Birth Outcomes after Deworming Pregnant Women. Pediatr Infect Dis J. 2006; 25(9):791-4. https://doi.org/10.1097/01.inf.0000234068.25760.97 PMid:16940835

29. Larocque R, Casapia M, Gotuzzo E, Maclean JD, Soto JC, Rehme E, Gyorkos TW. A double blind randomized controlled trial of antenatal mebendazole to reduce birthweight in a hookworm endemic area of Peru. Trop Med Int Health. 2006; 11(10):1485-95. https://doi.org/10.1111/j.1365-3156.2006.01706.x PMid:17002722

30. Christian P, Khatry SK, West KP Jr. Antenatal anthelminthic treatment, birth weight, and infant survival in rural Nepal. Lancet. 2004; 364: 981-983. https://doi.org/10.1016/S0140-6736(04)17023-2

31. Torlesse H, Hodges M. Albendazole Therapy and Reduced Decline in Haemoglobin Concentration during Pregnancy (Sierra Leone). Transactions of the Royal Society of Tropical Medicine and Hygiene. 2001; 95:195-201. https://doi.org/10.1016/S0035-9203(01)90164-6

32. The Urban Population of Calabar. GeoNames Geographical Database, updated March 2015.

33. Olusanya O, Okpere E.E, Ezimokhad M. The Importance of Social Class in Voluntary Fertility Control in a Developing Country. West African Journal of Medicine. 1989; 4(4):198.

34. Elliot AM, KIzza M, Quigley MA. The impact of helminthes on the response to immunization and on the incidence of infection and disease in childhood in Uganda: Design of a randomized, double-blind, placebo-controlled, factorial trial of deworming interventions delivered in pregnancy and early childhood. Clinical Trials. 2007; 4: 42-57. https://doi.org/10.1177/1740774506075248 PMid:17327245 PMCid:PMC2643383

35. Oladeinde B, Omoregie R, Oladeinde OB, Odia I. Prevalence of malaria and anaemia among pregnant women attending a Traditional Birth Home in Benin City, Nigeria. Oman Med J. 2012; 23(3): 232-236. https://doi.org/10.5001/omj.2012.52 PMid:22811774 PMCid:PMC3394357

36. Dim CC, Onah HE. The Prevalence of AnaemiaAmong Pregnant Women at Booking in Enugu, Southeastern Nigeria. Med J. 2007; 9(3):11.

37. Alem M, Enawgaw B, Gelaw A, Kenaw T, Seld M and Olkeba Y. Prevalence of Anaemia and Associated Risk Factors among Pregnant Women Attending Antenatal Care in Azezo Health Centre Gondar Town, Northwest Ethiopia. J Interdiscipl Histopathol. 2013; 1(3):137-144. https://doi.org/10.5455/jihp.20130122042052

38. Owolabi MO, Owolabi AO, OlaOlurun DA. Socio-demographic factors in anaemia in pregnancy in South-western Nigeria. S Afr Fam Pract. 2012; 54(3):222-227.

39. Yahya M, Brooks DR, Werier MM, Cabral C, Al-Shafei MA and Wallenburg HC. Effect of High Parity on Occurrence of Anaemia in Pregnancy: A Cohort Study BMC Pregnancy and Childbirth, 2011, 11:7. https://doi.org/10.1186/1471-2393-11-7 PMid:21251269 PMCid:PMC3033858

40. Kalaivani K. Prevalence and Consequences of Anaemia in Pregnancy. Indian J Med Res. 2009; 130: 627-633. PMid:20090119

41. Christian P, Khatry SK, West KP Jr. Antenatal Anthelminthic Treatment, Birthweight, and Infant Survival in Rural Nepal. Lancet. 1994; 364: 981-983. https://doi.org/10.1016/S0140-6736(04)17023-2

42. Torlesse H, Hodges M. Albendazole Therapy and Reduced Decline in Haemoglobin Concentration during Pregnancy (Sierra Leone). Transactions of the Royal Society of Tropical Medicine and Hygiene. 2001; 95:195-201. https://doi.org/10.1016/S0035-9203(01)90164-6

43. Geerts S, Gryseels B. Drug Resistance in Human Helminths: Current Situation and Lessons from Livestock. Clinical Microbiology Reviews. 2000; 13: 207-222. https://doi.org/10.1128/CMR.13.2.207-222.2000 PMid:10755998 PMCid:PMC100151