Anaemia in Women of Reproductive Age in Tanzania

A study in Dar es Salaam

BY

SIRIEL NANZIA MASSAWE
ABSTRACT


The overall aims of the study were to determine the prevalence of anaemia in women of reproductive age and to investigate the underlying causes, as well as assess the effectiveness of antenatal care (ANC) interventions for anaemia prevention. Consecutive pregnant women booking for ANC (n=2235) were screened for anaemia, followed up and screened again late in pregnancy. Basic ANC interventions included iron and folate supplementation, malaria chemoprophylaxis and referral of severe anaemia cases, and in addition staff training and education for the women and the community at the study clinic. Non-pregnant women (n=504), adolescents: pregnant (n=76), non-pregnant (n=130), and boys (n=101) were also screened for anaemia. Haematological and biochemical investigations were made on anaemic cases.

The prevalences of anaemia and severe anaemia in pregnant women were 60% and 3.8%, respectively. The adolescent pregnant women were more anaemic, with an overall prevalence of anaemia of 76%. In the non-pregnant women the prevalence was 49%. Anaemia was more prevalent in adolescent girls than in boys, and iron deficiency was the main underlying cause in all groups. In the anaemic pregnant women, malaria and other infections were more common, and Serum ferritin therefore underestimates iron deficiency.

ANC interventions achieved a significant reduction in the prevalence of severe and moderate anaemia but only a moderate reduction in overall prevalence of anaemia. Time for treatment of anaemia during pregnancy is inadequate to correct pre-existing nutritional deficiencies, and all the underlying factors are not addressed. Anaemia control must include all women of reproductive age, starting with adolescents to build up their iron stores before pregnancy. ANC supplementation should include other nutrients, and there is also a need to identify and treat infections during pregnancy. Training of ANC providers and supervision as well as improvement in the logistics and supply supplements to the clinics needs reinforcement.

Key words: Anaemia, pregnancy, reproductive age women, iron deficiency, intervention

Siriel Nanzia Massawe, Department of Women's and Children's Health, Section for International Maternal and Child Health (IMCH), Uppsala University, University Hospital, SE-751 85 Uppsala, Sweden

© Siriel Massawe 2002

ISSN 0282-7476
ISBN 81-554-5308-2

Printed in Sweden by Uppsala University, Tryck & Medier, Uppsala 2002
To my husband August, and to my children Furaha, Bumija, Clara and Cecilia.
This thesis is based on the following papers, which will be referred to in the text by their Roman numerals:


IV Massawe S, Ronquist G, Nyström L, Lindmark G. Iron status and sideropenic anaemia in adolescents in a Tanzanian sub-urban area. Submitted


Reprints were made by permission from the publishers
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>In plain text</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIDS</td>
<td>Acquired Immunodeficiency Syndrome</td>
</tr>
<tr>
<td>ANC</td>
<td>Antenatal care</td>
</tr>
<tr>
<td>BMI</td>
<td>Body Mass Index</td>
</tr>
<tr>
<td>DHMT</td>
<td>District Health Management Team</td>
</tr>
<tr>
<td>ELISA</td>
<td>Enzyme Linked Immune Adsorbent Assay</td>
</tr>
<tr>
<td>GNP</td>
<td>Gross National Product</td>
</tr>
<tr>
<td>Hb</td>
<td>Haemoglobin concentration</td>
</tr>
<tr>
<td>HIV</td>
<td>Human Immunodeficiency Virus</td>
</tr>
<tr>
<td>IEC</td>
<td>Information, education and communication</td>
</tr>
<tr>
<td>ITNs</td>
<td>Insecticide treated nets</td>
</tr>
<tr>
<td>MCH</td>
<td>Maternal and Child Health</td>
</tr>
<tr>
<td>MCHA</td>
<td>Maternal and Child Health Aid</td>
</tr>
<tr>
<td>MCH4</td>
<td>Maternal and Child Health Card number 4 (Ministry of Health Tanzania)</td>
</tr>
<tr>
<td>MCV</td>
<td>Mean corpuscular volume</td>
</tr>
<tr>
<td>MMC</td>
<td>Muhimbili Medical Centre</td>
</tr>
<tr>
<td>MMR</td>
<td>Maternal mortality ratio</td>
</tr>
<tr>
<td>MOH</td>
<td>Ministry of Health</td>
</tr>
<tr>
<td>PHC</td>
<td>Primary health care</td>
</tr>
<tr>
<td>RBC</td>
<td>Red blood cells</td>
</tr>
<tr>
<td>S-ferritin</td>
<td>Serum ferritin</td>
</tr>
<tr>
<td>S-CRP</td>
<td>Serum C-reactive protein</td>
</tr>
<tr>
<td>SSD</td>
<td>Sickle cell disease</td>
</tr>
<tr>
<td>STfR</td>
<td>Soluble transferrin receptor</td>
</tr>
<tr>
<td>TDHS</td>
<td>Tanzania Demographic and Health Survey, National Bureau of Statistics</td>
</tr>
<tr>
<td>TRCHS</td>
<td>Tanzania Reproductive and Child Health Survey, National Bureau of Statistics</td>
</tr>
<tr>
<td>UNICEF</td>
<td>United Nations Children's Fund</td>
</tr>
<tr>
<td>VHW</td>
<td>Village health worker</td>
</tr>
<tr>
<td>WBC</td>
<td>Total white blood cells</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organisation</td>
</tr>
</tbody>
</table>
INTRODUCTION

Anaemia - a general health problem
Anaemia is a major public health problem world-wide. It estimated that around 2 billion people, 30% of the world population, are affected (DeMaeyer & Adiels-Tegman, 1985), with the majority coming from the developing world. Infants, pre-school children, adolescents, and women of childbearing age, particularly pregnant women, are at greatest risk of developing anaemia. It is reported that 56% of pregnant women in developing countries and 18% in the developed countries are anaemic, and in Africa the estimated prevalence in pregnant women is 50%-60% (WHO, 1992). For the non-pregnant women the estimated prevalence is 43% and 12% in the developing and developed countries, respectively (WHO, 1992). Adolescents and school age children are also vulnerable groups, and an estimated 37% of school age children are affected. However, adult males may also be at risk, especially where there is inadequate food intake, and/or frequent parasitic infestations, a situation that is common in the developing countries. The estimated prevalences of anaemia for this group are 18% and 3% in the developing and developed countries, respectively (DeMaeyer & Adiels-Tegman, 1985). The causes of anaemia are multiple, but iron deficiency is by far the most important nutritional anaemia worldwide (DeMaeyer et al., 1989).

Anaemia, women and reproduction
Women have additional needs of iron requirements from puberty to menopause. These arise from the physiological requirements of menstruation, pregnancy and, to some extent, lactation. For this reason, iron deficiency is common in women of reproductive age even in developed countries (Katai et al., 1996; Milman et al., 1993), throughout their reproductive years. In pregnant women there is increased demand due to the physiological increase in maternal red blood cell mass, and the needs of the growing foetus and placenta. During adolescence, the growth spurt increases the need for iron, and, for the girl, there is further increase due to regular menstrual loss. In the developing countries, the high iron demands in these groups are not met, mainly because of the poor diet of low iron bio-availability, and frequent parasitic infections, thus leading to a high incidence of anaemia in women and girls. An adolescent who conceives soon after menarche is likely to start pregnancy with depleted stores. Adolescent pregnancies are common in developing countries and anaemia is one of the serious health problems for the girls (Arkutu, 1979; Brabin et al., 1998). Too many pregnancies that are closely spaced are also common in Africa, and put a heavy
nutritional demand on the woman who, after a pregnancy and lactation, has no time for physiological recovery before a subsequent pregnancy (Fleming, 1989b).

**Consequences of anaemia**

Anaemia has detrimental physical, social and economic effects. Even mild to moderate anaemia affects the sense of well-being, resulting in fatigue, stress, and decrease in work capacity.

Severe anaemia that occurs in developing countries is a major cause of maternal mortality and morbidity (Harrison & Rossiter, 1985; WHO, 1992). Anaemia is attributed as a direct or indirect cause of about 26% of maternal deaths in Africa. Severe anaemia may cause cardiac failure and death, whereas chronic anaemia is considered to be contributory, especially in cases of haemorrhage and infection. Furthermore, anaemic women are poor anaesthetic and operative risks, as anaemia may lead to poor healing of the wound and to increased susceptibility to infections (Brabin, 1985). The extent to which anaemia may cause maternal deaths is also dependent on availability and quality of obstetric services. Availability of blood transfusion is often lifesaving in cases of severe anaemia (Harrison & Rossiter, 1985).

Anaemia during pregnancy is also associated with an increased risk of intrauterine growth retardation, premature delivery and low birth weight, resulting in an increase in perinatal mortality (Brabin et al., 1990; Fleming, 1989b). Infants of anaemic women are born with reduced iron stores and are at risk of anaemia during infancy and increased risk of infant morbidity and mortality (Cook, 1994; Scholl et al., 1992). Reduction of anaemia during pregnancy is therefore a key component of safe motherhood.

**Main underlying causes**

Several factors are responsible for the high prevalence of anaemia in childbearing women, and they vary according to geographical location. During pregnancy there is an increased demand for nutrients as a result of the expanding maternal RBC mass and the needs of the growing foetus and placenta, and in between pregnancies the demands are increased by the iron loss due to menstruation (Brabin, 1985). In Africa, anaemia in women is caused by multiple factors (Fleming, 1989a).

**Iron deficiency**

In public health terms, iron deficiency is by far the most important cause of nutritional anaemia. Iron deficiency may result from a combination of several factors, including
(1) inadequate dietary intake and/or low dietary availability, (2) increased iron needs during pregnancy and periods of rapid growth such as adolescence, (3) chronic iron losses due to parasitic infections such as hookworm and schistosomiasis, and (4) impaired iron utilisation in chronic and repeated infections. Iron requirement during the second and third trimester is about 7 mg/day. This cannot be obtained, since the main source of iron in the diet in these countries is non-haeme iron. Its absorption is affected by meal composition, (commonly consumed foods contain phytates which are inhibitors of iron absorption) and therefore less bio-available (Cook et al., 1994). However, it is also reported that even in developed countries, where the diet quality is good, only 20% of women have normal iron stores at the end of pregnancy and postpartum in the absence of supplementation (Lindsay, 1997; Milman et al., 1999).

*Malaria*

There is increased susceptibility to malaria in pregnancy, which is greatest during the first half of pregnancy and in primigravida women. Most patients are relatively asymptomatic, and the main effect seen is anaemia. The haemolysis associated with malaria can also increase folate requirements, and where dietary intake of folate is poor, as is often the case, folate deficiency can exacerbate the anaemic state. Surveys in Africa where malaria, especially Plasmodium falciparum malaria, is endemic, show that it is a major contributing factor to severe anaemia in the primigravida, and also a significant risk factor for low birth weight (Brabin et al., 1990; Fleming et al., 1986). Interventions to reduce malaria during pregnancy will have significant impact on the health of the women and their newborn babies. Chemoprophylaxis with antimalarials during pregnancy is recommended, and has been shown to reduce both the prevalence of severe anaemia and of low birth weight, provided it is not started late in pregnancy (Fleming et al., 1986; Mutabingwa et al., 1993b). With the widespread chloroquine resistance there is increasing difficulty in the provision of effective chemoprophylactic regimes for pregnant women (Mutabingwa et al., 1993a).

*Folic acid deficiency*

Apart from deficiency associated with malaria, folate deficiency can also be caused by poor dietary intake alone, especially as folate-rich foods can be depleted of folate by prolonged cooking, which is common practice in much of tropical Africa. Pregnant women are prone to folate deficiencies because of high physiological requirements, and deficiency is especially common in multigravidae, twin pregnancies and also in the last trimester and in lactation (Fleming, 1989b).
Other nutrient deficiencies
There is a general consensus that in poor countries diets tend to be deficient in multiple micronutrients and not only iron and folate. Deficiency of vitamin B12, vitamin A, as well as zinc also contribute to anaemia but the extent of these deficiencies in the region has not been determined. The need for national research to determine the extent of these other deficiencies has been emphasised as it has implications on supplementation policies for vulnerable groups.

Parasitic infections
Hookworm infection is endemic in many tropical countries, and chronic blood loss due to hookworm is a significant contributor to anaemia, particularly moderate and severe anaemia. The degree of iron deficiency anaemia due to hookworm depends on the content and bio-availability of iron in the diet, the size of body iron stores, and the intensity and duration of the infection (Stoltzfus et al., 1997b). Trichuris trichura, Schistosoma haematobium, and Schistosoma mansoni may also contribute, but in isolation they are unlikely to result in severe anaemia.

Other chronic infections and inflammations
The possibility that chronic inflammatory disease plays an important aetiological role for anaemia of pregnancy in developing countries has not often been studied. Recently, however, studies have shown that infections could be an important factor associated with anaemia during pregnancy (Bondevik et al., 2000; van den Broek & Letsky, 2000). Current and chronic infections interfere with nutrient uptake and also depress bone marrow activity, resulting in anaemia. It is known that the immune status is altered during pregnancy and pregnant women are thus predisposed to various infections, and these infections are often occult and/or sub-clinical (Brabin, 1985).

HIV/AIDS is ranked high as determinant of anaemia in women, and its prevalence is increasing in women of reproductive age in sub-Saharan Africa (Fleming, 1997; UNICEF, 1998). Recent studies in areas with high HIV-1 sero-prevalence have reported that HIV-positive women have increased prevalence and severity of anaemia during pregnancy (Antelman et al., 2000; van den Broek et al., 1998). Opportunistic infections and dietary deficiencies in AIDS patients are associated with anaemia. Also, an independent effect of HIV infection on haemoglobin concentration that is not associated with concurrent infection or dietary deficiency has been demonstrated (van den Broek et al., 1998). Furthermore, HIV infection diminishes a pregnant woman’s capacity to control P. falciparum infection, further increasing the risk of anaemia (Shulman et al., 1999; van den Broek et al., 1998; Verhoeff et al., 1999).
Haemoglobinopathies

Haemoglobinopathies such as thalassemia and sickle cell disease are other known causes of anaemia reported in the region (Fleming et al., 1986). Where health services are inadequate, mortality is high among those with the severe type of haemoglobinopathy. With improvement in health care services, cases of severe sickle cell disease (Hb-SS) that affect about 1% of individuals, should also be expected among the anaemic cases during pregnancy.

Interventions for anaemia

The control of anaemia in women of childbearing age is a priority public health problem (WHO, 1992). Haematinic supplementation is recommended for all pregnant women in high anaemia prevalence areas in developing countries. This approach has had only limited success, except under well-controlled conditions. The reasons for this vary, but general problems are logistics to ensure availability and distribution of tablets within primary health care (PHC) settings of care, as well as inadequate supervision of providers (UNICEF, 1998; Yip, 1994). Problems of compliance with prophylactic medication by women are another possible contributing factor. Several studies have shown that logistic problems inherent in PHC programmes such as lack of supplies, distribution, supervision of health providers and adequate information to pregnant mothers were more significant (Galloway & McGuire, 1994). The other main reason for the limited success is that anaemia is prevalent even in non-pregnant women and the treatment period in pregnancy is too short to correct it. Furthermore, the often multifactorial causes of anaemia cannot be addressed by supplementation of iron and folate alone (Meda et al., 1996; Viteri, 1997b). For this reason, WHO recommended local studies to be undertaken for each region, to provide baseline information for design of prophylactic and therapeutic regimes (WHO, 1989).

General information about Tanzania

Social and demographic indicators

Tanzania is one of the least developed countries. The total population is about 33 million (as projected from the 1988 population census) with crude birth and death rates of 43 and 19 per thousand, respectively. The major health problems are mainly infectious diseases such as malaria, respiratory tract infection, diarrhoeas and tuberculosis. Recently HIV/AIDS is increasingly a priority health problem. Life expectancy at birth is 47 and 51 years for women and men, respectively. The inset illustrates some vital reproductive and general health indicators for Tanzania.
Total population       33 million*
Crude birth rate     46/1000**
Crude death rate     15/1000**
Population growth rate 2.8%**
Infant mortality rate 99/1000*
Under-five mortality rate 147/1000*
Contraceptive prevalence rate 16%*
Total fertility rate 5.6%*
Female literacy       60%*
Male literacy         69%*
% deliveries in a health facility 44%*
Maternal mortality ratio 770/100,000***

* TRCHS, National Bureau of Statistics, 1999
** National Bureau of Statistics, 1988
*** WHO, 1996

**Health services in Tanzania (Figure 1)**

Health services in Tanzania are organised according to a three-tier referral system. The lowest level is the village health post. At this level, a village health worker provides community-based basic health services. The next level is the dispensary and then the health centre. Both the dispensary and the health centre provide curative and preventive services. The health staffs at these levels are midwives, clinical officers and assistant clinical officers. The first referral level is the District hospital, which caters for about 250,000 inhabitants and is staffed in addition by a medical doctor or an assistant medical officer and trained nurse midwives. A medical doctor assisted by a District Health Management Team (DHMT) is in charge of all medical services, curative and preventive, at district level. With regard to maternity care, all pregnant women with complications during pregnancy labour, delivery and after, should be referred to the district hospital (i.e. obstetric first referral level). The government has adopted a policy of cost-sharing in health care as part of the health sector reform but maternal and child health (MCH) services are still free at all levels. The health sector is undergoing reforms in phases, which focus on decentralised management, diversification of health financing, and on public/private mix in the provision of health services (Ministry of Health, 1994). Management of health services is decentralised at district level, and the role of the MOH is the development of health policy and guidelines. The regional level provides a link between the MOH and the
Figure 1. Organisation of health service.

*MCHA – Maternal and Child Health Aid
A special cadre, basically trained to provide MCH-services
district level and the regional level has a function of overseeing health policy implementation and supervision in the districts within the respective region.

Antenatal services are provided through MCH clinics, which are present at all levels of health facilities and provide comprehensive services to the mother and child, including antenatal care (ANC), delivery care, postnatal care and family planning services, as well as under-five child immunisation and growth-monitoring. Antenatal coverage country-wide is 98% (TRCHS, 1999) and most ANC is provided at MCH clinics at PHC level. MCH aid is a special cadre of health workers specifically trained to provide services at PHC level. At the district hospital a nurse midwife would be in charge of the MCH clinic. 44% of women deliver at a health facility and 56% deliver at home (TRCHS, 1999). Utilisation of family planning services is low, with only 18% of eligible women benefiting from these services.

Anaemia in Tanzania

Data collected from health institutions in the country show that anaemia is one of the top ten health problems seen in outpatient clinics (Mnyika, 1991). Anaemia affected a significant proportion of in-patients in regional hospitals, especially of under-five children and pregnant women, and was an important cause of mortality in this vulnerable group. Further assessment of the anaemia situation, especially for the underlying causes, was limited by the inadequate laboratory facilities at all levels of health care (Mnyika, 1991). At the time of planning these studies, there was limited accurate information from the MCH clinics on the magnitude of anaemia in women because there are often no means for Hb assessment in most of the clinics. The national referral criteria for anaemia in pregnant women Hb $\leq 8.5$ g/dl assumes that means are available to screen for anaemia at the antenatal clinics. Studies made in Dar es Salaam in the early seventies showed that anaemia was universal in pregnant women along the coast region (Mwanukuzi & Nhonoli, 1972; Nhonoli, 1974).

Because of the high prevalence of anaemia in the region, and as recommended by WHO, a policy was adopted of prophylactic supplementation with iron and folic acid in antenatal clinics for all pregnant women, since the early seventies. Tablets should be distributed through the MCH system free of cost to all pregnant women. Subsequently it could be demonstrated by Nhonoli (1974) that prophylaxis with iron and folic acid, even for a limited time during pregnancy, led to improvement of haemoglobin in women.
However, over the years anaemia has continued to be a major cause of mortality and morbidity during pregnancy in Tanzania despite the supplementation. At Muhimbili Medical Centre (MMC), the national referral hospital, anaemia is one of the major reasons for maternal mortality and morbidity (Justsen, 1985; Mtimavalye et al., 1980), and this was still found in the early nineties (Urassa et al., 1996). Available studies on anaemia during pregnancy had been carried out in the early seventies (Mwanukuzi & Nhonoli, 1972; Nhonoli, 1974) and there was a need for updated information regarding the anaemia situation.

Situation regarding anaemia management in the study district
Before we started the main study, we performed a health facility survey to obtain information on anaemia screening, management and referral system in the study district, and the experiences of the mothers with the programme. Two clinics and the district hospital were visited and observations made regarding facilities for screening and treatment of anaemia during pregnancy. Health workers were interviewed to assess their knowledge and perception of anaemia in pregnancy as a health problem, its management and prevention. One hundred parous pregnant women who had registered for ANC at the three clinics were interviewed to assess their knowledge and experience of anaemia and their attitude towards supplementation. The antenatal clinic at the district hospital was also visited to assess the management of anaemia cases referred from the PHC clinics. The clinics had no means to screen for anaemia and there were problems with the supply of iron and folic acid tablets for supplementation and on the provision of information to the women on the need for supplementation. There were also no facilities for checking blood pressure and urine analysis. Even the district hospital lacked reliable anaemia screening and inadequate investigations and follow-up of referred cases. The results of the interview of pregnant women and the observations in the baseline study have been published (Massawe et al., 1995). These baseline observations formed the basis for the ANC anaemia intervention activities included in this thesis.

Aims for the studies
The overall aim was to study anaemia in women of reproductive age in Dar es Salaam and to investigate the major underlying causes in the anaemic women.

Specific objectives
- To assess the prevalence of anaemia in pregnant women, non-pregnant women and adolescents.
- To investigate the main underlying factors for anaemia in these groups.
To assess the effectiveness of existing antenatal interventions for anaemia prevention at PHC level, with the addition of a community-based health education on causes and prevention of anaemia in pregnancy.

SUBJECTS AND METHODS

Setting
Dar es Salaam region has three districts: Ilala, Kinondoni and Temeke, each with a district hospital. There are several peripheral PHC units, i.e. health centres and dispensaries, distributed throughout the districts. MCH clinics provide comprehensive care for the mother and baby, including ANC, postnatal care, family planning, and under-five immunisation and growth-monitoring and health and nutrition education. There is an MCH clinic at each level of health care. Figure 1 shows the organisation of MCH services. At the peripheral PHC clinics, a specially trained health cadre, MCH-aid, provides for low risk women and refers women at risk to the district hospital. The referral of at-risk mothers is according to criteria stipulated on the national antenatal card (MCH4). For anaemia during pregnancy the cut-off Hb level for referral and investigations is 8.5 g/dl, and this is clearly indicated on the national antenatal card (MCH4). The district hospital is the first referral level for maternity services, and MMC provides tertiary level services.

Study area
The studies were conducted in Temeke district, one of the districts in Dar es Salaam region. Two MCH clinics at PHC level in the suburban area of Temeke were selected for the study: Mbagala (the study clinic), which is fourteen kilometres from Temeke district hospital, and Kasarobo (the control clinic), three kilometres from the hospital. These clinics were chosen because they shared the same district hospital, were within reasonable distance for supervision by the study co-ordinators, and the staff was willing to cooperate. Each clinic provides ANC to the community in its catchment area and the distance between clinics was considered large enough to avoid effects of community information activities in the control area. We used the study clinic Mbagala for the assessment of anaemia in the non-pregnant women, and Mbagala primary school, which is within the catchment area of the study clinic, for the study on adolescents.
### Study design and subjects

The prevalence study was cross-sectional and the intervention study longitudinal. The characteristics of study subjects and study design are presented in Table 1.

<table>
<thead>
<tr>
<th>Study design</th>
<th>Setting</th>
<th>Subjects</th>
<th>Recruitment period</th>
<th>No. of cases</th>
<th>Age group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cross-sectional prevalence</td>
<td>MCH clinics</td>
<td>Pregnant</td>
<td>1991-92</td>
<td>2235</td>
<td>15-49</td>
</tr>
<tr>
<td>Longitudinal intervention in antenatal care</td>
<td>MCH clinics</td>
<td>Pregnant</td>
<td>1992-93</td>
<td>1045</td>
<td>15-49</td>
</tr>
<tr>
<td>Cross-sectional prevalence</td>
<td>MCH clinics</td>
<td>Non-pregnant</td>
<td>1995</td>
<td>504</td>
<td>16-45</td>
</tr>
<tr>
<td>Cross-sectional prevalence</td>
<td>MCH clinics</td>
<td>Primigravidae</td>
<td>1998</td>
<td>76</td>
<td>12-19</td>
</tr>
<tr>
<td>Cross-sectional prevalence</td>
<td>Primary school</td>
<td>Girls and boys</td>
<td>1999</td>
<td>234</td>
<td>12-19</td>
</tr>
</tbody>
</table>

### Field work and data collection

**Anaemia prevalence in pregnant women in Dar es Salaam, 1991-92**

Consecutive pregnant women during their first ANC visit to Mbagala (study) and Kasarobo (control) clinic were invited to participate and they gave consent. Recruitment took place between June 1991 and June 1992. A research midwife interviewed them, and data on their age, parity, occupation, and educational level were recorded, and Hb assessed. Gestational age was assessed from the last menstrual period, and when it was uncertain an estimate was made using the fundal height in each case. They had their height and weight checked using a scale, which had an in-built adjustable height measure. None of the women took iron medication before booking. Recruited women were followed up during pregnancy.
**Intervention in antenatal care and follow-up, 1991-1993**

Interventions based on the pre-study results (Massawe et al., 1995) included supply of iron and folate tablets, chloroquine tablets, information to mothers, appropriate means to screen for anaemia, and increased knowledge of ANC staff on anaemia in pregnancy, its prevention and treatment. For ethical reasons some of the interventions had to be introduced also at the control clinic. Table 2 summarises the interventions that were carried out throughout the study period at the clinic and at the community level. The rationale for the specific interventions described below in the study clinic area was to improve knowledge and awareness of anaemia as a health problem in both mothers and ANC staff as well as in the community, and to encourage early booking for ANC.

<table>
<thead>
<tr>
<th>Table 2. Intervention activities for anaemia carried out at the study clinic (intervention area) and control clinic</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intervention activity</strong></td>
</tr>
<tr>
<td><strong>In both clinics</strong></td>
</tr>
<tr>
<td>Provision of sphygmomanometer, weighing scales</td>
</tr>
<tr>
<td>and albustix</td>
</tr>
<tr>
<td>Provision of HemoCue haemoglobinometers and</td>
</tr>
<tr>
<td>training of MCH-aides on its use to estimate Hb</td>
</tr>
<tr>
<td>Provision of iron, folic acid, and chloroquine</td>
</tr>
<tr>
<td>tablets on a regular basis</td>
</tr>
<tr>
<td><strong>In study clinic only</strong></td>
</tr>
<tr>
<td>Training seminars for MCH-aides on causes,</td>
</tr>
<tr>
<td>prevention and treatment of anaemia</td>
</tr>
<tr>
<td>Individual counselling - when issuing tablets</td>
</tr>
<tr>
<td>Audio cassette messages on anaemia at the clinic</td>
</tr>
<tr>
<td>Leaflets and posters on anaemia in pregnancy</td>
</tr>
<tr>
<td>Community-based meetings/dialogues within the</td>
</tr>
<tr>
<td>clinic catchment area on all aspects of anaemia</td>
</tr>
</tbody>
</table>

**Specific study area interventions**

*Seminar for ANC staff at Mbagala clinic*

The six MCH aides at Mbagala clinic participated in a one-day seminar on anaemia as a health problem: causes, consequences and prevention; importance of screening; referral; routine supplementation and counselling of each woman.
**Subjects and methods**

**Audiocassette messages at Mbagala clinic**
Summarised messages on anaemia in pregnancy were repeated daily at the clinic, after the regular health education message had been given by the MCH staff, while the women were waiting for their turns to be attended to.

**Leaflets and posters at Mbagala clinic**
Posters were placed in each room at the clinic and leaflets were given to all women. The posters emphasised the importance of taking the tablets given at the clinic and the need for the family members to support the pregnant woman. The leaflets that were distributed had the same message on anaemia as the audiocassettes.

**Community health information programme in Mbagala ward**
The purpose of the community health education was to create awareness on anaemia during pregnancy; as a health problem, its causes, consequences and prevention, also at the community level. A total of eight meetings were held, in the four areas in Mbagala ward, and all the meetings were held in the evenings after four o'clock according to a previously agreed schedule with the community leader. The meetings lasted for about one and a half hours. The study team, together with the district gynaecologist, MCH co-ordinator, and the research midwife, conducted these meetings.

The target group included both men and women in the study area. The messages were conveyed in dialogue with the participants and the specific contents included:

- Underlying causes of anaemia, both nutritional and environmental.
- Consequences of anaemia to the mother and baby.
- Prevention of anaemia at community level.
- Importance of early booking for ANC.
- Importance of complying with haematinics that were supplied at the clinic. Iron and folic acid tablets, and chloroquine were shown to the people, with explanations on how to take them.

During the second round of meetings, four months after the initial visit, previous messages were reinforced, leaflets on anaemia were distributed and a poster was placed at the community leader’s office at each meeting place.

**Follow-up phase**
Follow-up continued until December 1993, when all women recruited had delivered. Our initial plan was to follow-up the women recruited up to the time of delivery and six weeks postpartum and record the delivery outcome. Unfortunately, the drop-out
rate was high as women in this community travelled during the last month of pregnancy to stay with a close relative in order to obtain support during labour and postpartum. Figure 2 shows the women that were recruited and followed-up. We were able to follow-up 50% of the women to late pregnancy; however, the statistics recorded on the women followed-up were similar to those who dropped out from the clinic (Table 3).

Figure 2. Flow chart of recruitment and followed-up to late pregnancy.
Table 3. Comparison of the median for some basic characteristics at booking for all registered women, and for those followed-up at gestational age ≥34 weeks

<table>
<thead>
<tr>
<th>Basic characteristic (median)</th>
<th>All registered (booking)</th>
<th>Follow-up ≥ 34 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>23</td>
<td>24</td>
</tr>
<tr>
<td>Parity</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Gestational age (weeks)</td>
<td>23</td>
<td>24</td>
</tr>
<tr>
<td>Level of education (years)</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>155</td>
<td>154</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>50</td>
<td>53</td>
</tr>
<tr>
<td>Body Mass Index</td>
<td>22.1</td>
<td>22.2</td>
</tr>
<tr>
<td>Haemoglobin (g/dl)</td>
<td>10.0</td>
<td>10.0</td>
</tr>
<tr>
<td>Number of ANC visits</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Number of women</td>
<td>2235</td>
<td>1045</td>
</tr>
</tbody>
</table>

The follow-up was done according to the ANC routines, i.e. every four weeks up to 28 weeks, fortnightly up to 36 weeks and weekly until delivery. Hb was measured at booking and every four weeks. All women were given ferrous sulphate 60 mg twice/day, folic acid 5 mg/day and chloroquine 300 mg/week. At each visit, women were asked to report if they had an attack of fever as a proxy for malaria, and if they had taken their tablets. An attempt to ask women to bring any tablets that remained at the next visit failed because many mothers forgot to bring them.

Treatment during follow-up

Women whose Hb was ≤8.5 g/dl were treated at the clinic and followed-up at two-weekly intervals. Treatment included ferrous sulphate 60 mg three times/day, folic acid 5 mg/day, and chloroquine treatment course (1500 mg in three days) followed by a chloroquine 300 mg weekly. Women who had severe anaemia (Hb persistently <7.0 g/dl) were referred for further investigations and treatment at MMC. All women, whose Hb dropped to ≤8.5 g/dl were investigated for the cause of anaemia, and the investigations done were as described below.
Outcome variables

- Haemoglobin late in pregnancy (gestational age ≥34 weeks).
- Percentage of women dropping below the cut-off level (Hb ≤8.5 g/dl).
- Percentage of women reporting fever attacks.
- Gestational age at booking.

Prevalence of anaemia in parous non-pregnant women, 1995

From May 1995 to Dec. 1995 consecutive women who had brought their children for vaccination and/or had come for family planning services at Mbagala MCH clinic were invited to participate in the study, after obtaining informed consent. Their obstetric history and socio-economic circumstances history were recorded, and they were screened for anaemia. A sub-sample of women with Hb <11.0 g/dl were further investigated to determine the cause of the of the anaemia by haematological and biochemical tests.

Prevalence of anaemia in nulliparous adolescent pregnant women, 1998

Consecutive primigravidae ≥20 years were recruited for the study during their first visit to the antenatal clinic between June and July 1998. A research midwife interviewed them and they were weighed and height was measured. Gestational age was assessed from the last menstrual period and if uncertain it was estimated by the fundal height. Venous blood was drawn for haematological and biochemical investigations. They were also screened for malaria and intestinal parasites.

Prevalence of anaemia in adolescents, 1999

Boys aged ≥12 years and post-menarcheal girls in Mbagala primary school were screened for anaemia after getting permission from the school authorities and individual consent. A research midwife interviewed them and their height and weight were measured. Venous blood was drawn for haematological and biochemical investigations and they were requested to submit a stool specimen for analysis of intestinal parasites.

Laboratory investigations

Haemoglobin measurements

Each clinic was provided with a portable HemoCue haemoglobinometer (HemoCue AB, Ängelholm, Sweden) and all the MCH aides at the two clinics were trained on how to use it to check for anaemia. The HemoCue haemoglobinometer uses disposable microcuvettes and a rechargeable battery. No dilution is required. The microcuvette is filled when it makes contact with a drop of blood and is then inserted into the meter and read after 45 seconds. The use of this method in outpatient clinics by non-
technical staff has been described (Schenk et al., 1986). The instrument has a coefficient of variation of 2% under standard conditions (Schenk et al., 1986). For the adolescents study, venous blood was drawn and transported for haematological analysis using the Coulter electronic machine at MMC.

Validation of haemoglobin measurements
The calibration of the HemoCues was checked daily using control microcuvettes provided by the manufacturer. The HemoCues at the two clinics were compared regularly using venous samples of known Hb value as determined by the Coulter counter. A specimen with Hb = 6.6 g/dl was run 25 times in each and another 25 measurements on Hb = 12.0 g/dl (Coulter) were run in each HemoCue. A comparison was also made between the two HemoCues and two health workers; each of them ran 19 samples on both.

The HemoCue calibration readings were according to the standards given in each case. The mean difference between measurements of the two HemoCues was 0.2 (p<0.005) and the mean intra-individual difference was 0.2 for both machines. For the specimen with Hb = 6.6 g/dl (Coulter) the readings were averaged 6.5 (range 6.3-6.7) on one HemoCue and 6.4 (range 6.2-6.7) on the other, and on the specimen with Hb = 13.0 (Coulter) the readings were 12.8 (range 12.6-13.2) on one and 12.7 (range 12.4-13.0) on the other. The coefficient of variation was 0.2 for both machines.

Handling of blood samples
During the study period, 2235 pregnant women from the two clinics were screened for anaemia. In a sub-sample, pregnant women with Hb ≤ 8.5 g/dl at HemoCue screening (capillary prick) at first or follow-up visits to the clinics (n=404), were further investigated. Venous blood samples were collected in standard tubes (Becton and Dickson) for further haematological (EDTA) and biochemical analysis (non-EDTA tubes), at the Central Haematology Laboratory at MMC. The specimens were processed within three hours of collection. Seven samples clotted and could not be further processed. Only venous samples with Hb <10.5 g/dl obtained by the Coulter electronic counter at MMC were included in the further analysis (n=351). Serum was separated and frozen at -20º C and was later transported for biochemical analysis at the Department of Clinical Chemistry, Uppsala University.

In a sub-sample of pregnant women with moderate to severe anaemia (n=71), bone marrow aspiration from the iliac crest was done using sterile technique under local anaesthesia. Stool samples for analysis of intestinal parasites were obtained from 231 anaemic women. From the study population (n=2235), 565 consecutive pregnant
women were investigated for malaria as a reference for malaria prevalence. In cases where pathology was found, appropriate treatment was prescribed.

*Other laboratory investigations*

Haematological investigations including red blood cell count (RBC) and mean corpuscular volume (MCV), and white blood cell count (WBC) were performed by the Coulter electronic system. The Coulter was calibrated daily by a standard according to the manufacturer’s instructions (Counter Electronics LTD). Peripheral smears for blood and bone marrow were stained by standard technique (May-Grünwald-Giemsa) (Dacie & Lewis, 1984). Bone marrow films were, in addition, stained by Perl’s Prussian blue reaction (Dacie and Lewis, 1984) for assessment of hemosiderin granules. HIV-1 serostatus was tested immunologically using the enzyme-linked immunoadsorbent test (ELISA) and was non-linked to individual identification.

Thick blood smears for malaria parasites were stained by a Giemsa technique (Dacie and Lewis, 1984) and an absolute parasite count was calculated from observed WBC (WHO, 1961). One technologist at MMC performed stool microscopy for intestinal parasites using standard routine procedure. Serum was analysed for ferritin (S-ferritin) (n=248) and C-reactive protein (S-CRP) (n=211) at the Department of Clinical Chemistry, Uppsala University, using immunological techniques, S-CRP being assayed by an immunological turbidimetric method, and S-ferritin by 2-point fluoroimmunometry based on a direct sandwich technique. These investigations could not be performed on all samples due to inadequate specimens and spillage during transportation. The mean Hb value and the proportion of cases with severe anaemia were very similar in all subgroups, so there was no indication of selection bias. For S-ferritin the recommended WHO cut-off for assessment of S-ferritin in developing countries, <50 µg/l, was used (WHO, 1989), and for S-CRP a cut-off of >10 mg/l was used (Romen & Artal, 1985).

Venous blood specimens were also collected from a sub-sample of anaemic non-pregnant parous women (n=71) for haematological investigations and biochemical analysis. For the adolescent groups (boys, non-pregnant girls and pregnant adolescents), (n=307), S-ferritin and S-CRP, serum transferrin receptor (sTfR), were also analysed at the Department of Clinical Chemistry Uppsala University, in addition to haematological investigations. sTfR was measured immunoenzmetrically using
JDeA™ sTfR kits (Orion Diagnostics), and the reference interval was set at 1.3-3.3 mg/l. There were no differences between sexes.

**Definition of anaemia**

We adopted the WHO definition of anaemia in pregnancy as Hb <10.5 g/dl in women in the second trimester and severe anaemia as Hb <7.0 g/dl (WHO, 1993). For those pregnant women investigated to determine the underlying cause for the anaemia, the operational cut-off value of 8.5 g/dl for antenatal clinics in Tanzania was used. For the non-pregnant women and adolescents the WHO cut-off value of Hb <12.0 g/dl was used.

**Statistical methods**

The Quest statistical and epidemiological software was used for data entering and analysis of the study of pregnant and non-pregnant women, and the EpiInfo 6 programme was used for the adolescent study. Student's t-test was applied for the differences in arithmetic means, and the medians and Pearson's Correlation coefficient for the linear relationship between variables. Chi-square test with Yate’s correction was used for the comparisons of proportions. Multiple regression analysis was used in trying to explain the variation between Hb and maternal characteristics.

**Ethical considerations**

A full explanation of the purpose of the study and the investigations to be carried out was given to all study participants. Informed consent was obtained in each case. Whenever pathology was detected, appropriate treatment was given and/or referral advised.

The Muhimbili University College Research and Ethics Committee, and the Ethics Committee of the Medical Faculty, Uppsala University, granted ethical clearance before the studies.

**RESULTS**

**Anaemia in pregnant women (Paper I)**

Two thousand two hundred and thirty-five pregnant women (1391 and 844 from the study and the control clinic, respectively) were assessed for anaemia. Their median age was 23 years, and median gestation age was 23 weeks. Ninety-seven percent were housewives, and 26% had never attended school. The median Hb was 9.8 g/dl in Mbagala and 10.4 g/dl in Kasarobo, and the overall prevalence of anaemia
Anaemia in women of reproductive age in Tanzania

(Hb <10.5 g/dl) was 60% and severe anaemia (Hb <7.0 g/dl) was 4%. There was a statistically significant (p<0.001) difference in the prevalence of anaemia between the clinics (49% vs. 66%) in Mbagala. Nearly 20% had Hb <8.5 g/dl, and required referral to a district hospital for further investigations and treatment according to MCH4 referral criteria.

Haemoglobin level according to age, parity, gestational age and BMI

The prevalence of severe anaemia was significantly higher in women below 20 years of age (6.1%) as compared with women 30 years and older (3.6%) (p<0.001), as well as in nulliparous compared with parity 1 to 4 (6.2% vs. 2.7%)(p=0.012). Further the prevalence of severe anaemia increased with increasing gestational age from 2.3% in women booking before 18 weeks to 6.7% in women booking week 30 or later, but the difference was not statistically significant (p =0.113). The association between BMI and Hb was tested for those registering before 24 weeks, (before any pronounced pregnancy weight gain occurs in a population like this). The mean BMI was 22, and a low BMI (≤19) was not statistically associated with more severe anaemia (Figure 3).

All the maternal characteristics, (age, gravity and parity, weight and height, systolic and diastolic blood pressure, gestational age at booking and educational level) were included as independent variables and Hb as dependent variable in a multiple regression analysis. However, the maternal characteristics, weight, gestational age at booking, and parity explained only 2% of the variation in Hb.

Effectiveness of antenatal care interventions (Paper II)

One thousand and forty-five pregnant women (684 and 361 from Mbagala and Kasorobo clinics, respectively) had their haemoglobin measured late in pregnancy (gestational age ≥ 34 weeks). The drop-out rate was high, most likely due to migration of women to visit their families in other parts of the country (Figure 2). Comparison of the basic characteristics of women followed–up showed that they were similar to the group originally recruited (Table 3). Therefore the analysis was made on the group followed–up to late pregnancy. The median time of follow-up during pregnancy was 14 weeks. The median Hb-values at booking and at last visit were 10.1 g/dl and 10.6 g/dl, respectively. The median increase in Hb of 0.5 g/dl was significant (p<0.005), and was similar in both clinics.

There was an overall reduction in the prevalence of anaemia from 60% to 47% late in pregnancy in both clinics, with 57% reduction in the proportion with severe anaemia (Figure 4). Women who had severe anaemia at booking, had a significantly (p<0.005)
Figure 3. Prevalence Hb ≤ 6.9, 7.0-10.4 and ≥ 10.5 g/dl at booking (n=2235) by BMI (≤ 19, 20-23, ≥ 24).

Figure 4. Reduction in prevalence of anaemia from booking to late in pregnancy (≥ 34 weeks) (n=1045).
higher increase in Hb late in pregnancy (median increase in Hb=3.2 g/dl), while non-anaemic women showed a significant (p<0.005) decrease (Median Hb=0.5 g/dl (Figure 5). The proportion with Hb ≤8.5 g/dl, i.e. those who would have required referral, was significantly reduced from 19% to 7.9% in the study clinic (p<0.001) and from 13% to 5.3% in the control clinic (p<0.001) (Table 4). Overall prevalence of anaemia Hb <10.5 g/dl was 60% at registration and 47% (p<0.001) at follow-up. The reduction observed was similar in magnitude in both clinics.

There was no difference in Hb levels late in pregnancy between those who reported fever episodes and those who had no such experience. Women who were still mildly anaemic late in pregnancy also had a lower initial median Hb at booking (9.7 g/dl vs. 10.5 g/dl) and significantly (p<0.001) more were severely anaemic at booking in this group, 3.5% vs. 0.9%.

Figure 5. Median Hb at booking and late in pregnancy (≥34 weeks) by Hb at booking (n=1045).
Table 4. Percentage of women with haemoglobin (Hb) level <7.0, ≤8.5, <10.5 and percentage reduction from booking to late in pregnancy (≥34 weeks), and the p-value for test of difference in prevalence between booking and late in pregnancy by clinic. Total period, during intervention (June 1991-Jan 1992)

<table>
<thead>
<tr>
<th>Hb-level (g/dl)</th>
<th>Mbagala clinic</th>
<th></th>
<th>Kasorobo clinic</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>At booking (p-value)</td>
<td>At booking (p-value)</td>
<td>≥34 weeks Reduction (%)</td>
<td>≥34 weeks Reduction (%)</td>
</tr>
<tr>
<td>Total: &lt;7.0</td>
<td>2.8 (0.052)</td>
<td>1.1 (0.704)</td>
<td>1.2 (0.052)</td>
<td>0.8 (0.704)</td>
</tr>
<tr>
<td>≤8.5</td>
<td>19 (0.001)</td>
<td>13 (0.001)</td>
<td>7.9 (0.001)</td>
<td>5.3 (0.001)</td>
</tr>
<tr>
<td>&lt;10.5</td>
<td>65 (0.003)</td>
<td>51 (0.003)</td>
<td>54 (0.003)</td>
<td>39 (0.003)</td>
</tr>
<tr>
<td>No. of women</td>
<td>684</td>
<td>361</td>
<td>684</td>
<td>361</td>
</tr>
</tbody>
</table>

Community education intervention
The community showed a high level of enthusiasm for the health messages. They freely asked questions, but men asked more questions than women did, and the research team had an opportunity to explain how anaemia affects women and that other groups such as children and men could also be affected. Discussions focused on the underlying causes of anaemia and on possible preventive measures. Emphasis was given to the importance of early booking, improved nutrition of pregnant women and the importance of taking the tablets given at the clinic. Overall, men expressed understanding and willingness to support anaemia prevention activities such as improved diet of pregnant women, early attendance to antenatal clinic and adherence to haematinics. The people found the information given to be useful, but since no community baseline data were collected before the start of the information programme, it was not possible to independently monitor the community effect of the programme.

Anaemia in non-pregnant parous women (Paper III)
Five hundred and four non-pregnant parous women from Mbagala clinic were screened for anaemia. Their median age was 25 years (range: 16-45), median parity was 2 (range: 1-13), and median education was seven years. Only one percent was formally employed. Their background socio-economic and obstetric characteristics were similar to the pregnant women investigated from the same study area (Paper I).
Nearly 80% were still breast-feeding their babies and the median age of the youngest child was 14 months. None of the women had any medical complaint. Figure 6 shows the distribution of Hb among non-pregnant (n=504) and pregnant women (n=1391) screened from Mbagala clinic. As expected, the median Hb in the pregnant women screened in mid-pregnancy was significantly lower, than in the non-pregnant women (9.8 vs. 12.0 g/dl) (p<0.001).

The prevalence of anaemia in the non-pregnant women was 49% and that of severe anaemia 1.6%. There were no statistically significant differences in the prevalence of anaemia with respect to socio-economic or obstetric characteristics, but anaemia decreased significantly with increasing BMI (p=0.042; Chi-square test for trend). Out of 504 women, only 143 (29%) were using hormonal contraceptives, mainly the pill (n=88) and Depo Provera (n=49), and the prevalence of anaemia was lower, among users although the difference did not reach statistical significance.

**Anaemia in among adolescents (Paper IV)**

A total of 307 adolescents were screened for anaemia, 101 boys, 130 non-pregnant girls and 76 pregnant adolescent (nulliparous) women. The median age was 14 years for both boys and girls and 19 years for the pregnant adolescents. Figure 7 shows the frequency distribution of haemoglobin in the three groups of adolescents. The majority (76%) of the nulliparous pregnant women were anaemic (Hb <10.5 g/l) and 10.5% were severely anaemic (Hb <7.0 g/l). The prevalence of anaemia Hb <12.0 g/l was 7.9%, and 14.6%, respectively among the boys and girls with 1.5% and 2.0% severely anaemic (Hb <7.0 g/l). Anaemia was also more prevalent among the older adolescents (16-18 years) compared with the younger ones, <16 years (21.7% and 13.1%, respectively).

**Underlying causes for anaemia (Papers III, IV & V)**

Further investigations for the main underlying cause for the anaemia were made for the various anaemic subgroups, as follows: pregnant women (n=361), anaemic non-pregnant parous women (n=71), pregnant adolescents (n=58) and non-pregnant adolescents (n=19), and boys (n=8) as shown in Table 5. Overall, iron deficiency was the predominant underlying factor identified in all anaemic groups. Figure 8 shows the prevalence of MCV <80 fl among the anaemic groups, and Figure 9 shows the percentage with S-ferritin below the cut-off level for iron deficiency. Intestinal worm infestations, mainly hookworm, were found in all the groups. Among the anaemic
Figure 6. Distribution of haemoglobin (Hb) level (g/dl) in pregnant (n=1391) and non-pregnant (n=504) women, visiting Mbagala clinic.

Figure 7. Frequency distribution of haemoglobin in the three groups of adolescents.
Table 5. Results of laboratory investigations made in the anaemic sub-groups

<table>
<thead>
<tr>
<th></th>
<th>Parous women</th>
<th>Adolescent girls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pregnant*</td>
<td>Non-pregnant**</td>
</tr>
<tr>
<td>No. of cases</td>
<td>351</td>
<td>71</td>
</tr>
<tr>
<td>Iron deficiency markers, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MCV &lt;80 (fl)</td>
<td>59.0</td>
<td>44.8</td>
</tr>
<tr>
<td>S-ferritin &lt;30, &lt;50 (µg/l)</td>
<td>76.0</td>
<td>70.7</td>
</tr>
<tr>
<td>sTfR &gt;3.3 (mg/l)</td>
<td>ND</td>
<td>29.3</td>
</tr>
<tr>
<td>Bone marrow hemosiderin negative, %</td>
<td>86</td>
<td>ND</td>
</tr>
<tr>
<td>Infections and elevated S-CRP, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malaria</td>
<td>33.5</td>
<td>51.7</td>
</tr>
<tr>
<td>Hookworm</td>
<td>21</td>
<td>25.9</td>
</tr>
<tr>
<td>HIV</td>
<td>7.4</td>
<td>ND</td>
</tr>
<tr>
<td>S-CRP &gt;10 (mg/l)</td>
<td>42.0</td>
<td>37.9</td>
</tr>
</tbody>
</table>

ND = not done, * Paper V, ** Paper III, *** Paper IV

pregnant women, presence of hookworm was significantly associated with severe anaemia, and also with negative bone marrow hemosiderin (Paper V). Malaria was significantly (p<0.001) more prevalent among the anaemic women compared with the reference pregnant population, and nulliparous women had significantly (p<0.001) higher prevalence of malaria compared with other parities (Paper V). There was no association between the level of haemoglobin and the malaria parasite count. Among the anaemic adolescent primigravidae, malaria parasites were present in over 52%, compared with 17% (p=0.019) prevalence among the non-anaemic primigravida (Paper IV). Iron deficiency was prevalent also in the anaemic and non-anaemic boys.

In 7% of the anaemic pregnant women investigated, there were megaloblastic changes in the bone marrow, suggestive of folic acid deficiency, and these were also associated with assessment of macrocytic changes in the peripheral blood film (Paper V). The contribution of undetermined infections to the anaemia was more common among the anaemic pregnant women and we found elevated markers of inflammation and infections in serum. Serum C-reactive protein (S-CRP), an acute phase reactant protein, was elevated (>10 mg/l) in 42%, compared with 8.7% among the
Results

Figure 8. Prevalence of MCV <80 fl in pregnant and non-pregnant parous women and adolescent girls and adolescent boys.

Figure 9. Prevalence of S-ferritin <50 (women), <30 (girls and boys) µg/l in pregnant and non-pregnant parous women and adolescent girls and adolescent boys.
non–pregnant women (Papers III, IV & V), and in 38% of the anaemic pregnant adolescents compared with 21% among the anaemic girls (Figure 10). S-ferritin is also an acute phase reactant that may reflect an ongoing inflammatory process. High S-ferritin was significantly (p<0.001) associated with elevated S-CRP, which means that S-ferritin in this population underestimates the degree of iron deficiency. High S-CRP was also associated with presence of malaria parasites (p<0.001) but not with presence of intestinal parasites, and a high eosinophil count (>4%). HIV-1 was positive in 6% of the anaemic women, which was similar to the prevalence of HIV-1 in the pregnant population in Dar es Salaam at the time of the study (Urassa et al., 1991). Presence of non-specific infections, as reflected by elevated S-CRP, was also more common in the pregnant adolescents compared with the non-pregnant (Paper IV).

We used sTfR, which is not an acute phase reactant (Carriaga et al., 1991; Ferguson et al., 1992), in addition to S-ferritin to assess the iron status in the adolescent subgroup. In the anaemic boys and girls, there was a statistically significant inverse correlation between S-ferritin and sTfR concentration (r=−0.39) (p<0.05). In the anaemic pregnant adolescent, this correlation was weak, and was not statistically significant (Paper IV).

Figure 10. Prevalence of S-CRP >10 mg/l in pregnant and non-pregnant parous women and adolescent girls and adolescent boys.
DISCUSSION

Maternal health care services
In a recent Tanzania Reproductive and Child Health Survey (TRCHS, 1999), ANC utilisation was 98%, and the median number of antenatal visits was four. It is of interest to note that this trend of high ANC attendance has persisted since the early nineties. On the other hand, the proportion of women delivering in health institutions has been declining over time, from 53% in 1991-92 to 47% in 1996 to 44% in 1999 (TRCHS, 1999), and only a minority of the women receive postnatal care. The high utilisation of ANC is also in sharp contrast to the high maternal mortality ratio (MMR) in the country, being among the highest in the world (WHO, 1996).

In the current debate on the effectiveness of ANC, it is emphasised that anaemia is one of the health problems that should be addressed (Rooney, 1992; Villar & Bergsjo, 1997). The ANC system in Tanzania has the potential to address the problem in view of the high utilisation.

The bulk of ANC service is provided at PHC level. At this level the main function is provision of routine care for low risk women, and identification of those with pregnancy complications to refer them to a district hospital. In principle, the health centre (HC) should have more functions. In practice, with regard to ANC, there is little difference in the level of care between the HC and the dispensary, and the next level of referral should therefore be the district hospital. Assessment of the anaemia situation in women of reproductive age in the country, and on the interventions that are possible within the health care system, must be done in the context of the maternal health organisational structure depicted in Figure 1. The pre-study survey of the health facilities identified some of the constraints for routine anaemia prevention programme in ANC at PHC level (Massawe et al., 1995), and these were addressed in the intervention part of the study as shown in Table 3.

Anaemia among pregnant women
Our studies demonstrate that anaemia is highly prevalent among pregnant women in Dar es Salaam. Already at booking for ANC, 60% were anaemic and 4% severely anaemic. More recent studies confirm the high prevalence of anaemia during pregnancy also in other regions in the country (Bergsjo et al., 1996; Hinderaker et al., 2001; Msolla & Kinabo, 1997; Tatala et al., 1998). These findings are in agreement with studies made in other developing countries (Haidar et al., 1999; Kuvidibila et al., 1991; Meda et al., 1996). The situation with regard to
Anaemia in the country has not changed over the last two decades (Mwanukuzi & Nhonoli, 1972; Nhonoli, 1974). In the Dar es Salaam area, based on clinical observations and on antenatal referrals to the tertiary hospital, there are suggestions that the problem of anaemia during pregnancy could be on the increase. Earlier studies on maternal mortality in Tanzania (Armon, 1979; Justsen, 1985; Mtimavalye et al., 1980), as well as more recent ones (Macleod & Rhode, 1998; Urassa et al., 1996), highlight anaemia as a major cause of preventable mortality in women.

Overall, women booked late for ANC (median booking gestation was 23 weeks). For the assessment of anaemia, therefore we used the recommended lower cut-off level of Hb <10.5g/dl, which takes into account the expected plasma volume expansion during pregnancy (WHO, 1993). Consistent with other studies, anaemia was more prevalent, and more severe late in pregnancy (Dreyfuss et al., 2000; Nhonoli, 1974) reflecting a deterioration of the anaemia as pregnancy advances, and in the absence of treatment. In addition, in developing countries, anaemia is common even among non-pregnant women, and anaemia develops rapidly because in most cases iron stores are depleted even before a pregnancy starts (Lamparelli et al., 1988; Meda et al., 1996; WHO, 1993). Young and nulliparous women were more severely anaemic. This is most likely due to the effect of malaria, which is endemic in the area. Peak malaria parasitaemia with resulting anaemia occurs at around twenty weeks in primigravida (Brabin, 1983; Fleming, 1989b). We found severe anaemia to be even more common among adolescent primigravidae (Hb <7g/dl in 10.5%), and this is in agreement with other studies conducted in the region (Brabin et al., 1998; Shulman et al., 1996). In this group, in addition to the effects of malaria, the increased nutritional requirements for the pregnancy are superimposed on the requirements for growth of the adolescent. Community education for early booking should be promoted to enable early treatment of anaemia and timely provision of malaria chemoprophylaxis. The challenge for the ANC is to provide quality services that will encourage women to report early for care.

Anaemia among non-pregnant women
Forty-nine percent of the non-pregnant parous women (80% lactating) were anaemic and nearly 2% severely anaemic (Kitange et al., 1993). Similar high prevalence rates were also found in two areas in Dar es Salaam, and in Lindi, a southern coastal district of Tanzania, respectively (Tatala et al., 1998). Our findings are in agreement with findings from other parts of the region, namely, Nigeria (Isah et al., 1985), Burkinafaso (Meda et al., 1996) and from Zimbabwe (Sikosana et al., 1998). The factors contributing to the anaemia were similar to those in the pregnant women, although the anaemic non-pregnant women had fewer infections associated with the
anaemia (elevated CRP > 10 mg/l in 8.7% compared with 42% in the anaemic pregnant women). The results emphasise the need to intervene and prevent anaemia in women, in between pregnancies. Although it has been a WHO recommendation to supplement women during lactation in areas with a high prevalence of anaemia, in practice only pregnant women are targeted in many countries (UNICEF, 1998; Viteri, 1997a). The rationale for control of anaemia in non-pregnant women has been to prevent maternal anaemia, in a subsequent pregnancy. However, other functional consequences of anaemia and iron deficiency, which include fatigue and reduced productivity should also be considered. In a study conducted in Indonesia, anaemia was associated with reduced productivity of women workers even in less strenuous tasks, which may include housework and childcare, or other income generating activities (Scholz et al., 1997). This has adverse economic impact for the individual, the family and the community. Prevention of anaemia would thus improve the physical well-being of both pregnant and non-pregnant women.

Women of childbearing age are at risk of iron deficiency throughout their reproductive years and not only during pregnancy. For this reason, a lifecycle approach for the control of anaemia in women of reproductive age in developing countries has been emphasised (UNICEF, 1998; Viteri, 1997b). Supplementation with iron should include adolescent girls and non-pregnant women during the lactation period. Implementation of this approach would ensure that women have adequate iron stores before a subsequent pregnancy, and improve the effectiveness of anaemia prevention during pregnancy.

The care of the mother and the baby has been promoted by WHO in the Mother-Baby package (WHO, 1994), and has been emphasised in the national Tanzania essential reproductive health care package. The women were studied when they came to the health system (MCH), for immunisation of their babies, and would have needed a general health screening and treatment themselves, but the post-natal care of women is not organised, and the coverage is very low (TRCHS, 1999). The results of this study emphasise the need to utilise the already existing contacts with women during the postnatal period, to treat and prevent anaemia and to promote their general health. Use of family planning should also be more actively promoted in Tanzania, as the coverage is currently low. Furthermore, the use of hormonal contraceptives is protective against iron deficiency in women (Milman et al., 1993) and if promoted could contribute to reduction of anaemia in women.
Anaemia among adolescents

Anaemia is reported to be the largest nutritional problem among adolescents in developing countries (Kurz, 1996). In this study, adolescent girls were more anaemic than boys. Only post-menarche girls were included and thus the findings reflect the increased requirement for iron in girls as a result of menstruation (Paper V). However, in both groups more than fifty percent of the anaemic and non-anaemic groups were iron-deficient. A study in Mwanza, and in Lindi region showed an even higher prevalence of anaemia, and iron deficiency among adolescent school children (Lwambo et al., 2000; Tatala et al., 1998). Inadequate dietary intake, as well as the intestinal parasites, especially hookworm that is endemic in the study area, contribute to anaemia and iron deficiency in this group (Stoltzfus et al., 1997a; Tatala et al., 1998). The results of our study highlight the need for intervention to improve the iron status in adolescents. Anaemia and iron deficiency are associated with low cognitive functions and educational achievement, and reduced physical fitness and immunity to infections (Nelson, 1996; Nokes et al., 1998). Improvement of iron status could minimise such adverse consequences. Recent studies in Tanzania documented improvement in growth and haematological parameters after weekly supplementation of the school children (Mwanri et al., 2000) and adolescent girls (Beasley et al., 2000). In the female adolescent, supplementation will also improve iron balance before pregnancy (Beard, 2000; Lynch, 2000) and minimise the possibilities of adverse pregnancy outcome.

Periodic de-worming through the school system is another approach that is recommended in areas with high hookworm prevalence. In Zanzibar, 4-monthly school based de-worming was found to reduce the incidence of severe anaemia (Hb <7g/dl) by 55% (Stoltzfus et al., 1998). In addition, the school system should be utilised to promote anaemia-preventive activities in the communities.

In a recent study in Tanzania, pupils and parents were found to have inadequate knowledge of anaemia even though the teachers had adequate knowledge. The study emphasised the need to strengthen the school health education programme as well as involvement of the parents and the general community in health and nutrition promotion (Mwanri et al., 2001).

Anaemia prevention and treatment in antenatal care

Currently, the policy in Tanzania is to supplement all pregnant women with iron and folate tablets. The results of this study support this approach, since the proportion of women with anaemia is so large that all pregnant women are at risk of anaemia and
Discussion

should be supplemented. This antenatal intervention is generally recommended for areas with high prevalence of anaemia in developing countries (WHO, 1993). However, anaemia remains a global health problem in women and supplementation programmes have had limited effect (Galloway & McGuire, 1994). Some of the main reasons for the limited effect of supplementation include logistic problems of supply and distribution of tablets, low coverage of target population, lack of motivation of health workers, and low compliance by pregnant women (Schultink et al., 1993; Viteri, 1994; Yip, 1994). In an earlier study in Dar es Salaam (Nhonoli, 1974) it was demonstrated that supplementation with iron and folate could be beneficial to women, even when received only for a short time. In his study, the mean Hb values of booked pregnant women who were given iron and folate tablets were significantly higher than that of the unbooked women at the time of delivery.

In the context of the study area, the identified constraints were addressed, as well as provision of basic equipment for routine ANC. The interventions were aimed at reinforcing the existing system and assessing the effectiveness, with the addition of community information in the study clinic area. As shown in Table 4, a significant reduction in the overall prevalence of anaemia and of severe anaemia late in pregnancy was observed both at the study clinic and at the control clinic. Women who were severely anaemic at booking had a significantly higher increase in median haemoglobin. Those who had a normal Hb at booking did not change. Women with a more severe anaemic condition experience improvement of symptoms and they are more motivated to take their tablets, furthermore iron absorption is increased in severely iron-deficient individuals. These findings are consistent with results of other studies (Koblinsky, 1994; Pappagallo & Bull, 1996; Zavaleta et al., 2000). There was a significant reduction in the prevalence of anaemia and severe anaemia observed at both clinics. This emphasises that the reinforcement of the interventions that was done at this level of health care during the study period were effective.

Overall, 47% of the women were still mildly anaemic late in pregnancy despite supplementation; most of these were moderately anaemic also at booking. The treatment given managed to avoid deterioration of the haemoglobin, but not normalisation. The duration of supplementation is also important. Pregnancy is too short a window for supplementation and when women are seen late in mid trimester, when already anaemic, too little is being done and also too late (Yip, 1996). Early booking should therefore be promoted to ensure a longer treatment time. In a review of supplementation studies, improvement of Hb levels was larger, when both the dose was higher, the subject more anaemic and the duration of supplementation was longer.
Anaemia in women of reproductive age in Tanzania

(Sloan et al., 1992). Recent guidelines recommend a smaller dose for supplementation of pregnant women, i.e. 60 mg elemental iron/day (Stoltzfus et al, 1998) and 120 mg when iron deficiency is a problem in women who are not pregnant or when supplementation is not started at the beginning of the second trimester.

The investigations made on the anaemic women confirmed the complexity of the underlying factors for the anaemia in pregnant women that also needs to be addressed. Although iron deficiency was the main underlying factor for the anaemia identified, supplementation with iron and folate alone was probably not adequate. Other factors included malaria, undetermined infections, and hookworm infestation. Assessment of other nutrient deficiencies, such as vitamin A and vitamin B12, was not done. However, recent studies in the region (Msolla & Kinabo, 1997; Savage et al., 1994; van den Broek & Letsky, 2000), suggest that these deficiencies, that were previously thought to be rare during pregnancy, were common among anaemic pregnant women, and might have also contributed to the residual anaemia. The importance of adequate vitamin A status during iron supplementation has been emphasised (Ribaya-Mercado, 1997). It has been shown that vitamin A plays an important role in the haematological response to iron, and individuals deficient in vitamin A are more likely to be unresponsive to iron supplementation. Thus, in a population in which mild to moderate vitamin A deficiency is common, concomitant supplemental vitamin A enhances the haematological response to iron and folate supplementation (Ahmed et al., 2001; Suharno et al., 1993). The extent of possible vitamin A deficiency among women of reproductive age in Tanzania has not been studied, and there is a need for further research in this area.

Furthermore, at the time of the study, various degrees of chloroquine resistance had already been reported in the country (Mutabingwa et al., 1993a), and chemoprophylaxis with chloroquine was probably inadequate. To be more effective, interventions should address all the underlying factors and, based on the results of our studies, these should include more effective malaria treatment and chemoprophylaxis, and active treatment of infections, in addition to iron and folate supplements.

Implications for health care

We have shown that, reinforcement of ANC preventive routines, at primary level, resulted in significant reduction of severe and moderate anaemia in pregnant women, in both the study clinic and in the control clinic. Only severely anaemic cases not responding to treatment required referral. The clinics operated according to their normal routines, with extra supervision only to ensure availability of tablets, testing for
anaemia, and recording that was necessary for the study. This has implications for the safe motherhood programme. Severe anaemia contributes to maternal mortality, and reduction of severe anaemia should have an impact on the reduction of maternal mortality (Brabin et al., 2001; Rush, 2000). Reduction of moderate and severe anaemia in a population like this is also thought to be a realistic target that is possible to achieve at this level of health care (Beaton, 2000; Stoltzfus, 1997).

The implication for the health care system is the need for improved capacity to perform further investigations of anaemic cases in facilities at the referral level, as this is currently inadequate (Massawe et al., 1995; Mnyika, 1991). At national level policy, decisions will have to be made on the need to include other micronutrients in addition to iron and folate that might have contributed to residual anaemia, based on further national research on these aspects.

Effect of equipment and adequate supplies of tablets and supervision (improved facilities)

Even though the two clinics in our study were different with respect to the overall prevalence of anaemia, the staff in both clinics were motivated to provide the available services, and distribute the tablets to the women. Women were also attracted by the services as both clinics registered an increased number of women during the study period. It seems, therefore, that the basic equipment, constant regular supply, and supervision provided to these clinics are the most important explanations of the improvement in haemoglobin levels of the women and that the general community information programme was perhaps of less importance during the short period of the study.

Compliance to supplementation

Another possible explanation of the residual anaemia is non-adherence to the drugs. We attempted to document compliance by asking women to bring unused tablets at subsequent visits to the clinic, but this was unsuccessful as the women often forgot to bring the drugs. Some studies have reported poor compliance to iron and folate by pregnant women (Bondarianzadeh et al., 1998; Schultink et al., 1993). The main reason given for non-compliance is said to be the side effects of iron, and these are dose-related. In a study made in Tanzania (Ekstrom et al., 1996), 42% of pregnant women were compliant to the conventional iron tablets, compared with 61% of those given slow-release iron preparation (gastric-delivery system, GDS), which is reported to cause fewer side-effects (Cook et al., 1990). This study was done in an area of the country where anaemia was uncommon (Moller et al., 1989). Although non-compliance by pregnant women may also be a significant factor, it has also been found
in several studies that lack of supplies was an even more important reason for women to stop taking tablets (Galloway & McGuire, 1994; Kobylansky, 1994). Even though compliance can be improved by more appropriate counselling of the pregnant women on the need for supplements to prevent anaemia (Galloway & McGuire, 1994), further local studies should be made to determine other factors that affect compliance by women, as well as on appropriate ways to motivate women to take the tablets.

Dosage and frequency of supplements
Decreasing the dosage and frequency of iron supplementation is another strategy being promoted to improve the effectiveness of iron supplementation. In recent years, a number of study results have suggested that weekly iron supplementation was as effective as daily iron supplementation in raising Hb levels, in various groups at risk of iron deficiency anaemia (Liu et al., 1995; Ridwan et al., 1996; Schultink & Gross, 1999), and that the smaller dose administered in the intermittent regime was associated with fewer side-effects and thus better compliance. The effectiveness of the intermittent dosage regime has also been challenged, with the main argument that, based on the calculated increased physiological iron requirements in pregnancy, sufficient iron could not be supplied by the weekly regime (Galloway & McGuire, 1996; Hallberg, 1998). Because women in the developing countries are often anaemic and iron-depleted even before pregnancy, a larger dose for the supplementation has often been recommended (Stoltzfus & Dreyfuss, 1998; UNICEF, 1998; WHO, 1993). Thus far, the issue of iron-dosage and frequency of administration is still controversial. An expert review of studies conducted in developing countries on a weekly versus daily supplementation (Beaton & McCabe, 1999), as well as more recent studies, concluded that daily supplementation was better than weekly supplementation in pregnant women (Mumtaz et al., 2000). On the other hand, a prolonged intermittent regime might be of benefit to non-pregnant women and adolescents (Agdeppa-Angeles et al., 1997; Bothwel, 2000), although it is also suggested that further, better-designed, studies are needed to resolve the issue of intermittent versus daily dosages. In addition, whatever dosing schedule is adopted, the fundamental problems – lack of supplies, inadequate knowledge of health workers, and poor counselling of women – have to be addressed in order to improve the effectiveness of iron supplementation programmes.

Assessment of haemoglobin
Successful management of anaemia in pregnancy depends on reliable means for detecting anaemia, assessing its severity and monitoring response to treatment (Topley, 1986). Efforts should therefore be made at PHC level where the majority of the women attend for ANC to ensure that Hb estimation is done on all women. The HaemoCue haemoglobinometer used in this study was simple to use in the field. The
technique was easily taught to the MCH-aides, who are the main providers of ANC at PHC level. The inter-observer difference in measurements under supervised field conditions proved to be of no clinical significance. The main drawback of this method is the cost of the disposable microcuvettes. When there are no means for assessing anaemia the problem is often underestimated, and the severe cases that are at risk of complications might be missed. Clinical assessment for pallor has been shown to have low sensitivity, especially in pregnant women (Meda et al., 1996; van den Broek et al., 1999). If carefully done, including checking various sites for pallor, the sensitivity might be improved and the very severely anaemic cases will be identified (Stoltzfus et al., 1999). It remains to be established to what extent an approach like this can be sustained, and improved at a routine antenatal clinic. At the moment, very little clinical assessment is done at clinics in Tanzania (Massawe et al., 1995; Urassa et al., unpublished manuscript).

There is need for a simple, cheap, but accurate, method for estimation of haemoglobin concentration. The new WHO colour scale is simple, well-accepted and cheap, and studies have shown that it has a potential for use in screening for anaemia in antenatal clinics in settings where resources are limited (van den Broek et al., 1999). Screening for anaemia in pregnancy is useful for a variety of reasons. It may help to collect baseline data on prevalence of anaemia and severity in a given population, and to assess the effects of ANC interventions for anaemia. At PHC level, it is particularly useful for deciding whether referral is necessary for more detailed investigations and treatment. Recently, the WHO colour scale was validated and found to be useful in tropical field conditions (van den Broek et al., 1999), and its advantage over clinical signs confirmed (Ingram & Lewis, 2000). The cost of this new device is also reported to be affordable and should be made available to all MCH clinics. Provision of these essential facilities motivates women to attend the clinic, and also may improve compliance to treatment. In one study, women tested with HaemoCue and diagnosed as anaemic found supplementation more acceptable (Koblinsky, 1994). Testing would promote a better understanding of anaemia by women, and also improve the quality of ANC.

Effectiveness of interventions for anaemia at PHC level in Tanzania
The improvement in the overall health delivery care, especially maternal care, is essential if the policy of supplementation is to have the desired effect. In the context of PHC care in Tanzania, this translates to reinforcement of the programme with activities designed to improve the knowledge and skill of providers of ANC, provision of essential basic equipment, and supplies of drugs (iron and folate and malaria chemo-prophylaxis), in addition to regular supervision. The quality of obstetric care at
the first referral level also should be improved so as to motivate compliance to referral by both the staff at PHC level and by the pregnant women. Women who were referred to the district hospital, for example, did not comply because there was no further care anticipated. At the district hospital, anaemic women were not investigated and there was no follow-up, as was expected. Within ANC, the overall aim should be to correct the anaemia and maintain safe Hb levels throughout pregnancy and before labour starts. During labour, a severely anaemic woman is likely to go into cardiac failure, or die, even after an otherwise normal blood loss after delivery, because anaemia reduces the tolerance to blood loss. The absence of means to assess for anaemia in antenatal clinics in Tanzania is of great concern. A recent study that assessed the quality of ANC with regards to management of anaemia in rural antenatal clinics in Tanzania highlighted the persistent substandard care. Only 37% had Hb checked using the unreliable Tallquist method, and 10% of the anaemic women were diagnosed clinically. In addition, action was taken in only 4% of the anaemic women (Urassa et al., unpublished manuscript). It is also of much concern that a recent community survey in the country (TRCHS, 1999) showed that only 40% of the women attending ANC were either given or prescribed haematinics, and only 32% had access to antimalarial tablets.

Our experience from the field is that availability of means to assess anaemia (Hemocue Hemoglobinometer) motivated the health workers to improve care for the women (Paper II). Also in other similar situations, health workers and pregnant women appreciated having a method that gave actual measurement of Hb as opposed to inspection of conjunctiva (Koblinsky, 1994; van den Broek et al., 1999). The results of our study thus emphasise the need to improve the overall quality of care in the antenatal clinics, as an enabling environment to implement effective anaemia prevention activities. Training and retraining of health workers at all levels of anaemia prevention should also be emphasised to create awareness of anaemia in pregnancy, its relation to maternal and perinatal health as well as on the importance of ANC supplementation and counselling of women.

Other causes of anaemia

**Malaria**

Malaria causes severe anaemia especially in primigravidae. In this study, we found that the prevalence of anaemia was significantly higher, and the mean haemoglobin significantly lower in primigravida women with a positive malaria test at booking. These findings were consistent with other studies in the region, notably Kenya and Malawi (Brabin & Piper, 1997; Shulman et al., 1996). In addition, they were also iron-
Discussion

deficient (*Paper IV*). At the time of the study, chloroquine was used as chemoprophylaxis for all pregnant women. A high rate of chloroquine resistance was already reported, and research to identify an alternative drug was ongoing in the country, and in other parts of the region (Mutabingwa et al., 1993b). Intermittent presumptive treatment with sulphadoxine and pyrimethamine (S/P) has now been shown to be effective in the region (Shulman et al., 1999; Steketee, et al., 1996). Chemoprophylaxis with intermittent S/P has been adopted by the MOH, but implementation has been slow. The main reasons for the slow take-off seems to be logistic, as well as health workers’ lack of information on policy changes. Once operationalised, a close follow-up will be needed to monitor the effectiveness of the intervention. The primigravidae, is the target group for malaria chemoprophylaxis because of diminished immunity to malaria. However, HIV-positive pregnant women have also increased susceptibility to malaria irrespective of parity. In addition, the recommended two doses of S/P were found to be inadequate, and thus monthly doses have been recommended for the sero-positive pregnant women (Parise et al., 1998; van den Broek et al., 1998). In view of the high prevalence of HIV infections among pregnant women, there is a need for policy revision on malaria chemoprophylaxis, and to include all women.

Malaria control measures at community level are necessary and pregnant women should be informed on the need for personal protection from malaria. Use of insecticide-treated nets (ITNs) by pregnant women has been promoted and has been found to reduce malaria anaemia and associated reduction in low birth weight babies. The bed nets must be obtained by the target population, and also dipped at six-month intervals. Major impediments to their use have been identified and they include affordability of the net material and insecticide, ensuring effective treatments as well as retreatment with insecticide. A recent study in Tanzania showed that promotion of the use of ITNs targeted to pregnant women through MCH clinics reduced anaemia and the prevalence and density of malaria in pregnant women (Marchant et al., 2002). However, in this study only one quarter of the women presented to the clinic before 20 weeks. Malaria infection rates are highest during the first half of pregnancy and decrease progressively until delivery (Brabin, 1983). The impact of this approach is therefore not maximised unless ITNs are used throughout pregnancy. This emphasises the need for community education to promote use of ITNs by women of childbearing age as well as for undertaking promotional activities at the community, and involving other groups. In this study, the majority of the women depended on the husband or someone else to purchase the net.
HIV infection
The HIV-1 prevalence was 7% in the sub-sample of anaemic pregnant women investigated in 1992 and 15% in the parous pregnant women in 1995. The pregnant women were investigated during the early days of the epidemic, and none of the women had frank AIDS. Although the sample of non-pregnant women was small, (n=71), the HIV sero-prevalence was in agreement with the reported HIV-1 prevalence in pregnant women in Dar es Salaam of 12% (Karlsson et al., 1997), and reflects an escalation of the HIV epidemic in women of reproductive age in Tanzania. HIV-infected pregnant women are at an increased risk of anaemia, and severe anaemia (Antelman et al., 2000; van den Broek et al., 1998). The increased risk of anaemia is thought to be associated with a higher degree of severity of the disease. However, in populations with a high risk of exposure to infectious diseases, particularly malaria, the vicious cycle of infections, impaired immunity and anaemia may result in a stronger association between HIV infection and anaemia already at an earlier stage of the disease. 70% of people with AIDS are anaemic, and AIDS, TB and related infections are ranked high as major determinants of anaemia in reproductive age women in Africa (UNICEF, 1998). A study conducted in Kenya among admitted patients with anaemia showed that severely anaemic women of reproductive age were significantly more likely to be HIV-positive (Zucker et al., 1994).

Strategies to reduce HIV transmission in the country will have an impact on the prevalence of anaemia in women, especially during pregnancy. HIV infection has the potential of worsening pre-existing anaemia, and blunting erythropoietic activity response to haematinics prescribed during prenatal care. On the other hand, control of severe anaemia in women will minimise the risk of HIV transmission through blood transfusion, which is often a life-saving treatment for severe anaemia, especially in pregnant women. A study performed in Kigali, Rwanda, showed that among women of child-bearing age, HIV sero-prevalence was 45% among women who had been transfused and 28% among those never transfused (Fleming, 1997).

Infections and inflammations
The prevalence of infections was high among anaemic pregnant women (Paper V). Infections interfere with iron absorption and uptake in the bone marrow, and thus contribute to anaemia. Most likely sites of sub-acute and chronic infections could be in the urinary tract and in the respiratory tract, including TB. In Malawi, infections were common among both HIV-positive anaemic and negative anaemic women (van den Broek &Letsky, 2000). A general clinical screening for infections is usually not done in ANC at PHC level because the providers are often not adequately trained. Routine
testing of urine is not done because the facilities are not available. Emphasis should therefore be made on detection of symptoms and referral for further care. This will require training of the providers at primary level, to improve history-taking and examination of pregnant women. Research is needed to identify prevalent infections, as well as an appropriate treatment strategy that could be recommended, in the form of guidelines at PHC level. There are plans for reorganisation of ANC in the country in line with the WHO recommendation, and this could be an opportunity to emphasise this component during the training of providers on the new WHO antenatal package.

**Hookworm**

Hookworm is prevalent in the area (Tatala et al., 1998; Vaughan et al., 1973) and contributes to anaemia in various groups of the population including women and children. In the pregnant anaemic women studied in the area, presence of hookworm was associated with severe anaemia *(Paper V)*. Contribution of hookworm to anaemia is dependent on hookworm load. However, in the context of a poor diet and low body iron stores, light to moderate hookworm infection is sufficient to cause anaemia. In hookworm endemic areas, women of reproductive age are susceptible to anaemia because their iron stores are inadequate (Stoltzfus et al., 1997b). Fifty-six percent of cases with moderate to severe anaemia among non-pregnant women in Zanzibar were attributed to hookworm (Stoltzfus et al., 1997a). Hookworm control is therefore an essential component of anaemia control in Tanzania. This could be achieved through community education on sanitary practices and also periodic de-worming of groups vulnerable for anaemia, especially school children and pregnant women (UNICEF, 1998). De-worming of pregnant women has been shown to significantly increase the beneficial effects of iron supplementation on Hb concentration and iron status (Atukorala et al., 1994). For this reason we recommend inclusion of de-worming of pregnant women in Tanzania since it is currently not a routine practice. This is also in line with current recommendations on anaemia control strategies in areas where the prevalence of hookworm infection is greater than 20% (Stoltzfus & Dreyfuss, 1998; UNICEF, 1998).

**Investigations for anaemia at district level**

Interventions to prevent anaemia have to be based on an understanding of the underlying causes. Assessment of the relative importance of factors contributing is limited in developing countries due to lack of resources and facilities for investigations. However, some basic investigations are possible at district level in order to identify the main underlying factors for the anaemia. These would include malaria assessment, stools, urine and a peripheral blood smear for RBC morphology.
Interpretation of peripheral smears to determine the cause of anaemia under these conditions has been described by Topley (Topley, 1998). Further investigations would be done on refractory cases as indicated, and the need for referral to a tertiary facility would be identified. At the moment there are difficulties to undertake even these basic investigations at the referral facilities due to limited facilities and also inadequate personnel. The need to improve the capacity of health facilities for investigations of anaemic cases should be emphasised.

**Assessment of iron status**

In this study, we used S-ferritin and sTfR concentration for the assessment of iron status. S-ferritin is an acute phase protein and underestimates iron deficiency, when both iron deficiency and infection are present, and for this reason different cut-off levels have been recommended for the diagnosis of iron deficiency. WHO recommended a cut-off of S-ferritin of <50 µg/l for developing countries, with high prevalence of inflammatory conditions (WHO, 1989). In a study in which bone marrow aspirates were used as the standard to validate the use of S-ferritin in a population where infections are also prevalent, a cut-off of <30 µg/l was found to be a reliable diagnostic indicator for iron deficiency (van de Broek et al., 1998), and this is consistent with the findings by Mast (1998). Other studies have shown that transferrin receptor concentration is a specific marker of iron deficiency during pregnancy and that it is not affected by chronic infections and physiologic changes in pregnancy (Carriaga et al., 1991; Kuvibidila et al., 1994). However, studies from sub-Saharan Africa suggest that its use may be limited in pregnant women, and also in the presence of chronic inflammation and infections (Semba et al., 2000; van de Broek et al., 1998). In addition, it might also be unreliable in the presence of malaria infection (Mockenhaupt et al., 1999; Verhoef et al., 2001) but the findings have not been consistent across studies (Asobayire et al., 2001; Menedez et al., 2001; Williams et al., 1999). Further studies are therefore needed to validate the use of sTfR concentration, as an indicator of iron status, in populations with a heavy burden of concurrent infections. Assessment of stained bone marrow is most reliable, but it is invasive and expensive, and not suitable for screening purposes (Ahuwalia, 1998). Where available, S-ferritin using the cut-off <30 µg/l is recommended as a reliable indictor of iron status in developing countries (Semba et al., 2000; van de Broek et al., 1998).

**Experiences with the community information programmes**

A limitation of this part of our study is that we were unable to collect baseline data from the community that would enable separate monitoring of the community information programme. Such an approach was not logistically possible within the
short time available for the study. Our study had a main focus on activities in the health care system, for anaemia management and prevention during pregnancy. A pre-study interview of the pregnant women showed that they had limited knowledge of anaemia and that the main source of information was mainly the MCH clinic and also the radio (only women who have had at least one previous pregnancy were interviewed) (Massawe et al., 1995). The aim of the community, information programme was to increase awareness and knowledge, also of the family and community on issues of anaemia and again focusing on prevention of anaemia during pregnancy. Improved knowledge among family members, especially the husband, could influence the pregnant women's health-seeking behaviour, including the support and encouragement to comply with the supplements (Moore et al., 1991).

A community-based information and education programme on anaemia in pregnancy resulted in increased compliance of the pregnant women to iron supplements, although the improved supply and distribution of iron tablets in the community was thought to have had more impact (Koblinsky, 1994). There are very few studies that report on the impact of a community-based programme on the haemoglobin levels of pregnant women late in pregnancy. Abel (2000) reports on an intervention study that also included community information and education in the study area (in addition to iron and folate supplementation during pregnancy) over an eighteen-month period. In their study, interventions also included de-worming of the pregnant women, from the study community. Post-intervention, the prevalence of anaemia was significantly lower and the iron status significantly better among pregnant women from the study area compared with the control area during the third trimester. It is noteworthy that the overall prevalence of anaemia remained high (56.8% and 80.1% in the study and control clinics, respectively), and the mean S-ferritin was lower during the third trimester compared with the first trimester values, even at the intervention clinic. The effect of the community IEC was also not separately analysed and anaemia was not categorised according to the severity. The findings of their study also underline the limitation of interventions focusing only on the period during pregnancy.

Education of the whole community is important to create awareness on anaemia in pregnancy and to give information on how to deal with contributing, nutritional and environmental factors. This approach should be beneficial in the long-term perspective, but in the short-term we concluded that availability of supplementation to the individual woman, and counselling, seem to be the most important factors in ensuring safe Hb levels late in pregnancy.
Some of the anticipated changes, as a result of community IEC on anaemia might include a change in dietary habits, that discourages consumption of iron inhibitors and encourages consumption of fruits and vegetables that promote iron absorption, as well as changes in the health-seeking behaviour of pregnant women. We had expected at least an effect on time to come for ANC, but women continued to book late in mid-trimester in both clinics throughout the recruitment period, although the need to book early was emphasised in the community education meetings. Late booking reduces the treatment time, and in addition in the primigravidae, malaria will have exerted its effects (Fleming, 1989b; Mutabingwa et al., 1993a). It seems that women do not come before ‘quickening’ takes place, since this is the best confirmation of pregnancy. In the absence of a goal-oriented care at first visit to the clinic, this situation is likely to continue. In Zimbabwe, earlier booking was not achieved, inspite of an intensified educational campaign using all media (Munjanja et al., 1996). A follow-up qualitative study that explored the reasons for late booking, showed that fear of witchcraft was one of the explanations given for not reporting to the clinic early when the pregnancy was not obvious (Mathole et al., 2001 pers. comm.). In Tanzania there are no studies that have explored the health seeking behaviour related to ANC, and the persistent late booking is of concern.

To enable planning for more effective community IEC on anaemia prevention and management, there is a need to conduct further studies to explore the perception of the community and women in relation to timing of ANC, and incorporate this in community education programmes. It is also important to explore how the community and women perceive the ANC in terms of content and the overall quality. Other aspects that are important for anaemia control include the acceptability and perception of iron and folate supplements and anti-malarial chemoprophylaxis.

Community-based distribution
In addition to community education, alternative distribution channels for supplements could be used at community level. In Indonesia the provision of iron and folate tablets at community level (through TBAs) resulted in increased compliance, and in the Gambia a similar distribution, also resulted in improved reproductive outcomes (Koblinsky, 1994; Menendez et al., 1994). This approach should also be explored in Tanzania, because currently there are village health workers and TBAs who are linked to the formal health system, and are involved in other community-based health programmes, including family planning and HIV/AIDS prevention activities.
Study results and recommendations for further research

In Tanzania, more than 70% of women make four or more visits to the antenatal clinic. However, the majority book late, at around twenty-four weeks. The reasons for this have not been studied. Late booking minimizes the benefits to be obtained from anaemia-preventive interventions, because adverse perinatal outcomes are associated with maternal anaemia in early pregnancy. There is a need for studies to explore the reasons for late booking and on ways to encourage early booking.

Our study showed that ANC interventions resulted in significant reduction of prevalence of moderate and severe anaemia late in pregnancy. Despite iron and folate supplementation, 47% of the women had residual mild anaemia. Some of the reasons for this include the short treatment time due to late booking, other factors contributing to anaemia that were not addressed by the current interventions, as well as non-compliance to the supplements. Studies are needed to assess the contribution of other nutrient deficiencies such as vitamin A, and vitamin B12.

It is important to undertake studies to assess the perception of iron and folate supplementation by pregnant women and on the factors that affect compliance to the supplements. These factors could then be addressed to further improve the effectiveness of the ANC anaemia prevention programmes. It is also important to explore the overall community perception on the quality and content of ANC, and identify education and information needs for community-based anaemia preventive activities. Collaboration with other relevant disciplines such as socio-science and nutrition should be encouraged in order to obtain a broad-base community perspective.

We also found that undiagnosed and untreated infections contributed to anaemia among pregnant women. Further studies are needed to better define the role of infections in causation of anaemia, to identify the causes of these infections, and to recommend appropriate ways of treatment at primary care level.

Recently, concern has been expressed on the lack of studies documenting the adverse outcomes associated with anaemia during pregnancy. Because anaemia is highly prevalent in pregnant women in Tanzania, there is a need for designing a study on the outcome of pregnancy in anaemic women as well as assessing the effects of interventions on pregnancy outcome.
**Special problems for field research in developing countries**

In a developing country set-up, research is made difficult by the limited facilities and the poor infrastructure of health facilities. The health workers are also few, overworked and sometimes not adequately trained, and the continuity of care for the individual woman is usually not possible. The record keeping is often poor, and this makes it difficult to maintain research records. The extra work involved for the research therefore demands a lot of supervision, as well as provision of extra facilities. In addition, the people in these communities are very mobile, making long-term follow-up difficult. The problem of loss to follow-up is therefore to be expected.

For instance, in our study area women moved out to other districts late in pregnancy to stay with relatives for social support and or decide to go for delivery at another health facility. For this reason, the drop-out rate was high. Our initial plans were to follow-up women and check their Hb before delivery and six weeks postpartum as well as to document pregnancy outcome, and delivery complications, but this turned out not to be feasible.

**CONCLUSIONS**

These studies have confirmed that anaemia is a major health problem in women of reproductive age. It is more prevalent and severe during pregnancy. Because of the high utilisation of ANC, the health care system has a potential to treat and prevent anaemia during pregnancy and thus minimise the associated consequences.

The group with anaemia is so large that efforts must be made to ensure Hb testing for all pregnant women. Provision of a simple method to screen for anaemia at PHC level is essential for selection of cases of severe anaemia for referral and also for follow-up of treatment. At the referral level, facilities for further investigations of anaemic cases need to be improved.

It is essential to provide prophylactics to all pregnant women. However, early booking should be encouraged and the logistics of drug supply improved as well as retraining of health workers and improvement of performance supervision, as well as overall improvement of the quality of care in antenatal clinics. Counselling of women on the need for the supplements should be emphasised.
Supplementation during pregnancy alone is inadequate to improve the situation, there is a need to promote other strategies to improve the nutrition and general health before pregnancy. These should include supplementation of lactating women and adolescent girls.

Malaria is an important cause of anaemia and there is a need to ensure adequate malaria treatment and protection during pregnancy, especially in the primigravidae.

Education on anaemia prevention should be emphasised in the community in order to encourage dietary modifications and promote environmental control of infections contributing to anaemia. This needs to be carried out on a continuous basis and integrated with other ongoing community health programmes.

Diagnosis, treatment and prevention of infections need to be included in routine ANC.
ACKNOWLEDGEMENTS

I would like to express my sincere gratitude to all those who have in one way or another supported and contributed to this work:

To my husband and my children for support, patience and encouragement.

To Gunilla Lindmark, my main supervisor, for her skilled scientific guidance, friendship and support for the many years that we have worked together.

To Lennarth Nyström, my second supervisor for the statistical instruction and for the very careful checking of tables and reference lists.

To Gunnar Ronquist, co-author coordinating the laboratory investigations in Uppsala, for assistance with the interpretation of the laboratory values and skilled scrutiny of the manuscripts.

To Karin Törnblom for excellent secretarial assistance and for administrative arrangements during my stay in Uppsala. Thank you for taking such good care of me and on all the issues related to our collaboration.

To Rose Swai, the MCH coordinator, Temeké district, for assistance and support during the fieldwork.

To Angela Mkende, research midwife, for her dedicated supervision of data collection.

To all the MCHA at Temeké and Kasarobo clinic for their cooperation.

To Juliana Mlalasi, Deborah Runyoro, and Vicky Nalyanga for the laboratory work at the central laboratory MMC.

To all the women and the pupils for their willingness to participate in the study.

To colleagues at Department of Obstetrics and Gynaecology, Muhimbili University College of Health Sciences for their support.

To Muhimbili University College of Health Sciences, my employer, for permission to undertake the studies and for giving me leave of absence.
To colleagues and staff at Department of Women’s and Children’s Health, Section for International Maternal and Child Health (IMCH), Uppsala University for their friendship and support.

To Sida/SAREC for the financial support of the research work, and always being constructive and understanding in discussions and communications about proposals and contracts.
REFERENCES


Beard JL. Iron requirements in adolescent females. J Nutr 2000;130:440S-2S.


References


Lynch SR. The potential impact of iron supplementation during adolescence on iron status in pregnancy. J Nutr 2000;130:448S-51S.


Mumtaz Z, Shahab S, Butt N, Rab A, DeMuynck A. Daily iron supplementation is more effective than twice weekly iron supplementation in pregnant women in Pakistan in a randomised double blind clinical trial. J Nutr 2000;130:2697-702.


Ridwan E, Schultink W, Dillon D, Gross R. Effects of weekly iron supplementation on pregnant Indonesian women are similar to those of daily supplementation. Am J Clin Nutr 1996;63:884-90.


