Perinatal mortality and anaemia in pregnancy in rural northern Tanzania

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University of Bergen

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   Blood and urine examinations – Sven Gudmund Hinderaker
   Mother and child – Bjørg Evjen Olsen
Back: Weighing pregnant women – Sven Gudmund Hinderaker
   Three other pictures by Bjørg Evjen Olsen

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To my dear mother.

You have twice lost a baby in the perinatal period. You understand the pain of the families I met who had experienced a perinatal death.
Table of contents

Table of contents .................................................................................................................................................. iv

List of figures ......................................................................................................................................................... vi

List of tables ......................................................................................................................................................... vi

List of maps .......................................................................................................................................................... vi

Abbreviations ....................................................................................................................................................... vii

List of original papers ........................................................................................................................................ viii

Acknowledgements ............................................................................................................................................ ix

Summary ............................................................................................................................................................... xii

1 Introduction ...................................................................................................................................................... 1

1.1 Reproductive health .................................................................................................................................... 1

1.2 Global strategies to achieve healthy reproduction .................................................................................. 2

1.2.1 Perinatal and neonatal mortality ........................................................................................................ 5

1.2.2 Anaemia in pregnancy ....................................................................................................................... 8

1.3 The Reproductive Health Project in Mbulu and Hanang districts ......................................................... 12

2 Aims and objectives ....................................................................................................................................... 15

3 Description of study area ............................................................................................................................. 17

3.1 Tanzania ................................................................................................................................................... 17

3.1.1 Health system in Tanzania ............................................................................................................. 18

3.2 Mbulu and Hanang districts and the study area ..................................................................................... 19

3.2.1 Infrastructure ..................................................................................................................................... 20

3.2.2 Cultural characteristics .................................................................................................................... 21

3.2.3 The health services in the study area ............................................................................................. 24

3.2.4 Health and disease in the study area ............................................................................................. 26

4 Subjects and methods ................................................................................................................................. 31

4.1 Selection of subjects ............................................................................................................................... 31

4.2 Study design ............................................................................................................................................. 32

4.2.1 Paper I : Perinatal mortality ............................................................................................................... 32

4.2.2 Paper II : Avoidable stillbirths and neonatal deaths ....................................................................... 33

4.2.3 Paper III: Anaemia in pregnancy .................................................................................................... 34

4.2.4 Paper IV: Determinants of anaemia in pregnancy ........................................................................... 34

4.2.5 Study power ....................................................................................................................................... 35
List of figures

Figure 1. Illustration of terminology applied to fatal events in the first year of life................................... 6
Figure 2. Monthly rainfall and temperatures in Haydom, 1995. ............................................................20
Figure 3. Perinatal mortality rate at Haydom Lutheran Hospital 1992-99. ............................................ 26
Figure 4. Malaria cases and deaths due to malaria at Haydom Lutheran Hospital, 1990-2000. ............28
Figure 5. Proportion of HIV-positive among blood donors at Haydom Lutheran Hospital. .................. 28
Figure 6. Outline of the study populations and selection procedures. ................................................... 31
Figure 7. Altitude correction factor for Hb (g/l) to be added to the measured Hb. ............................... 39

List of tables

Table 1. Infant mortality rate trends in the world, in deaths per 1000 live births................................. 5
Table 2. The most common causes of death among hospital admissions at the Haydom Lutheran
Hospital, 1995........................................................................................................................................ 27
Table 3. The most common diseases diagnosed at the outpatient department of the Haydom Lutheran
Hospital, 1995, Tanzania ................................................................................................................. 27
Table 4. Prevalence of anaemia in cross sectional and “nested” case control selection.................... 35
Table 5. Study power (1-\(\beta\)) to detect associations between determinants and anaemia (Hb < 90 g/l),
according to the odds ratio of the determinants. ............................................................................. 35
Table 6. Abnormal values for laboratory methods used....................................................................... 37
Table 7. Selected kappa values for validation of the antenatal questionnaire, assessed on interviews
of 58 of the pregnant women............................................................................................................. 38
Table 8. Selected studies on perinatal and neonatal mortality in Tanzania and eastern Africa........... 59
Table 9. Main causes of perinatal deaths.............................................................................................. 64
Table 10. Studies on the prevalence of anaemia in Tanzania............................................................. 65

List of maps

Map of Tanzania................................................................................................................................. 16
Map of study area .............................................................................................................................. 25
### Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>AC</td>
<td>Arm circumference</td>
</tr>
<tr>
<td>AIDS</td>
<td>Acquired immunodeficiency syndrome</td>
</tr>
<tr>
<td>ANC</td>
<td>Antenatal care</td>
</tr>
<tr>
<td>AOR</td>
<td>Adjusted odds ratio, “risk”</td>
</tr>
<tr>
<td>BS</td>
<td>Thick blood slide</td>
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<tr>
<td>CI</td>
<td>Confidence interval</td>
</tr>
<tr>
<td>CBR</td>
<td>Crude birth rate</td>
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<tr>
<td>CDC</td>
<td>Centers for disease control and prevention</td>
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<td>COSTECH</td>
<td>Commission for science and technology, Tanzania</td>
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<tr>
<td>CRP</td>
<td>C-reactive protein</td>
</tr>
<tr>
<td>CSSC</td>
<td>Christian social services commission</td>
</tr>
<tr>
<td>DDH</td>
<td>Designated district hospital</td>
</tr>
<tr>
<td>DH</td>
<td>District hospital</td>
</tr>
<tr>
<td>DMO</td>
<td>District medical officer</td>
</tr>
<tr>
<td>ELCT</td>
<td>Evangelical Lutheran church of Tanzania</td>
</tr>
<tr>
<td>END</td>
<td>Early neonatal deaths</td>
</tr>
<tr>
<td>FIGO</td>
<td>The international federation of gynecology and obstetrics</td>
</tr>
<tr>
<td>Hb</td>
<td>Hemoglobin</td>
</tr>
<tr>
<td>Hct</td>
<td>Hematocrit</td>
</tr>
<tr>
<td>HELLP</td>
<td>Syndrome with hemolysis, elevated liver enzymes, low platelets</td>
</tr>
<tr>
<td>HIV</td>
<td>Human immunodeficiency virus</td>
</tr>
<tr>
<td>HLH</td>
<td>Haydom Lutheran hospital</td>
</tr>
<tr>
<td>HSR</td>
<td>Health sector reform</td>
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<tr>
<td>ICD 10</td>
<td>International classification of diseases, tenth revision</td>
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<td>ICPD</td>
<td>International conference on population and development</td>
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<td>LD</td>
<td>Lactate dehydrogenase</td>
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<tr>
<td>LND</td>
<td>Late neonatal deaths</td>
</tr>
<tr>
<td>MCH</td>
<td>Mother- and child health</td>
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<tr>
<td>MMR</td>
<td>Maternal mortality ratio</td>
</tr>
<tr>
<td>OR</td>
<td>Odds ratio, “risk”</td>
</tr>
<tr>
<td>PMR</td>
<td>Perinatal mortality rate</td>
</tr>
<tr>
<td>RHP</td>
<td>Reproductive health project in Mbulu/Hanang</td>
</tr>
<tr>
<td>SB</td>
<td>Stillborn</td>
</tr>
<tr>
<td>STD</td>
<td>Sexually transmitted diseases</td>
</tr>
<tr>
<td>Tf sat</td>
<td>Transferrin saturation</td>
</tr>
<tr>
<td>UNFPA</td>
<td>United Nations Population Fund</td>
</tr>
<tr>
<td>UNICEF</td>
<td>United Nations Children’s Fund</td>
</tr>
<tr>
<td>UTI</td>
<td>Urinary tract infections</td>
</tr>
<tr>
<td>VDRL</td>
<td>Venereal diseases research laboratory test, unspecific syphilis test</td>
</tr>
<tr>
<td>VHF</td>
<td>Very high frequency</td>
</tr>
<tr>
<td>WB</td>
<td>World Bank</td>
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<tr>
<td>WBC</td>
<td>White blood cells</td>
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<td>WHO</td>
<td>World Health Organization</td>
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List of original papers


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Summary

The aim was to estimate the perinatal mortality rate, to study potential determinants and causes of perinatal and neonatal deaths, and their avoidability in a rural area of Tanzania. Further, we studied the prevalence of anaemia in pregnancy and the determinants of anaemia in pregnancy.

Attendants of the existing Mother- and child-health (MCH) clinics in the area run by the Haydom Lutheran Hospital were registered on their first antenatal visit and followed up one month after birth. Those who disappeared were traced to their home. In the cohort of 3618 women, some women were not possible to find (106) and 3512 were followed up and identified. Spontaneous abortion was reported in 42 cases, 3359 had a living baby, 53 had a still birth, 42 had an early neonatal death and 16 had a late neonatal death.

We studied the causes of stillbirths and neonatal deaths and their avoidability in the cohort. To secure a more complete picture, we also included deaths identified in a household study of 1259 homes in the same area: 6 stillbirths, 8 early neonatal deaths and 7 late neonatal deaths. The MCH attendants (n=3836) were studied cross-sectionally for prevalence and determinants of anaemia in pregnancy. Also, based on their hemoglobin (Hb) value, we selected 153 controls and 159 cases of anaemia with varying severity “nested” within the cohort, for a study to evaluate micronutrients and infections as determinants of anaemia.

The perinatal mortality rate (PMR) in the cohort was 27/1000 births, 56% were stillborn and 44% were early neonatal deaths. There was increased risk of perinatal death among babies with low birth weight and among women with a positive s-VDRL (Venereal Disease Research Laboratory). Women who had previously lost a baby and very lean women were also at higher risk.

Still births and neonatal deaths were often related to infection (39%), asphyxia (24%) or immaturity (15%). Among these deaths, 15% were estimated to be probably avoidable and a further 10% possibly avoidable, under the prevailing circumstances. Among the potentially avoidable stillborns and neonatal deaths, a patient-oriented avoidable factor was present in 51%, and a provider-oriented factor in 65%. Very few of the women were aware of their risk factors.

The mean Hb of the pregnant women was 12.1 g/dl, and 4.5% of them had Hb below 9.0 g/dl. The mean Hb was higher among persons living at higher altitude and at higher maternal age, and was lower during the malaria-season, and among women with malaria parasitaemia.
Anaemia among pregnant women was associated with iron deficiency, folate deficiency, and vitamin A deficiency. It was also associated with elevated C-reactive protein (likely infection) and elevated Lactate dehydrogenase (hemolysis, likely due to malaria infection). It was also associated with general signs of undernourishment (a small arm circumference).

The estimated PMR in this setting was lower than what has been found for other areas of Tanzania. This might be attributed to a well functioning health system in the area. The MCH had a high attendance of pregnant women, and although the referral to higher level was low, the existing MCH familiarized the women with the health system and made it more natural to be admitted to hospital if needed for delivery. Still, at least a quarter of the deaths in the study could have been avoided under the prevailing circumstances. The MCH should make sure that messages are understood and referrals accomplished.

Anaemia in pregnancy was less prevalent than in other areas of Tanzania. Common risk factors of anaemia were deficiencies of iron, folate, vitamin A, and infections, including malaria.
1 Introduction

1.1 REPRODUCTIVE HEALTH

In many societies, to marry and have children is the very meaning of life. Human reproduction gives social status, produces a work force and represents investment in the future, as well as securing succession of the family. The healthy outcome of a pregnancy is often regarded as a gracious gift, since the hazards are often observed and feared. Various traditional methods are used to secure a favourable outcome, e.g. traditional medicine, prayers, and witchcraft. Childlessness may be interpreted as a divine punishment, whereas many children may be a sign of blessing.

Box 1. Definition of reproductive health.
The following definition was endorsed by 165 countries at the International Conference on Population and Development (ICPD) in Cairo, 1994:

Reproductive health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity, in all matters relating to the reproductive system and to its functions and processes. Reproductive health therefore implies that people are able to have a satisfying and safe sex life and that they have the capability to reproduce and the freedom to decide if, when and how often to do so. Implicit in this last condition is the right of men and women to be informed and to have access to safe, effective, affordable and acceptable methods of family planning of their choice, as well as other methods of their choice for regulation of fertility which are not against the law, and the right of access to appropriate health-care services that will enable women to go safely through pregnancy and childbirth and provide couples with the best chance of having a healthy infant.

In line with the above definition of reproductive health, reproductive health care is defined as the constellation of methods, techniques and services that contribute to reproductive health and well-being by preventing and solving reproductive health problems. It also includes sexual health.

Source: ICPD 1, § 7.2

Reproductive health outlines health related aspects of human reproduction and addresses the reproductive processes, functions and systems at all stages of life. The definition stated in Box 1 is useful for high-income countries, because it encompasses all health-related aspects of human reproduction. However, in a poor setting, the main focus is on the survival of the pregnant women and their offspring. Other matters of reproductive health are naturally given
lower priority than survival. Globally, the major hazards threatening the life of pregnant and delivering women and their offspring are hemorrhage (25%), sepsis (15%), abortions (13%), eclampsia (12%), obstructed labour (8%), other direct causes (8%), and indirect maternal deaths (20%)\(^2\). Infection with Human Immunodeficiency Virus (HIV), malaria and severe anaemia may lead to indirect maternal deaths. According to estimates of the World Health Organization (WHO), half a million women die every year from these causes and many more suffer severe morbidity from their consequences\(^2\). The death of a mother severely jeopardises the survival chances of her offspring\(^3\). For the neonates, the major hazards in a global perspective are infection related (42%), asphyxia related (21%), immaturity related (10%), and congenital malformations (11%)\(^4\).

The global strategy to secure healthy reproductive outcomes is based on human rights and equity and rests on four pillars: 1) care for the women during pregnancy and childbirth; 2) care for the newborn; 3) control of sexually transmitted diseases; and 4) family planning\(^5\).

### 1.2 GLOBAL STRATEGIES TO ACHIEVE HEALTHY REPRODUCTION

In 19\(^{th}\) century Europe, the maternal and perinatal/neonatal mortality rates were similar to the rates in many developing countries today. During the last decades of that century, Sweden managed to reduce maternal mortality substantially by focusing on skilled birth attendants at community level, whereas the countries insisting on deliveries being conducted by specialists only (most of Europe, USA), lagged behind\(^6\). The improving socio-economic conditions were essential for the reduction of infant mortality, but seemed not to affect maternal mortality. However, the interventions in Sweden to reduce maternal outcome also seemed to reduce perinatal mortality\(^7\), suggesting that maternal mortality is closer related to perinatal mortality than to infant mortality.

The core of the antenatal care programs was developed in the early 20\(^{th}\) century. The pre-defined screening of pregnant women by a series of examinations at different stages of gestation was designed to detect conditions that threatened the pregnancy. This should in theory enable health personnel to treat and monitor these complications to secure a better outcome, and was later called the “risk approach”. The contents and timing were most often not scientifically evaluated\(^8,9\). Most developing countries inherited the European health systems during colonial times, and health care provision, including the antenatal care, was usually hospital or facility based.
During the 1970s, the Primary Health Care concept with preventive health services and community involvement was emphasised, as pronounced in the Alma Ata declaration of 1978. It led to a shift from facility based to decentralised, community based health care provision. Mother-and child health (MCH) care was one of the essential components of the strategy.

The efforts had little impact on the maternal mortality. As a consequence, the Safe Motherhood Initiative was launched at the Safe Motherhood Conference in Nairobi in 1987, through a collaboration between several agencies: the World Health Organization, United Nations Population Fund (UNFPA), the World Bank, the United Nations Children’s Fund (UNICEF), the International Federation of Gynecology and Obstetrics (FIGO), and others. Their ambitious initial goals were to reduce the maternal mortality ratio to 50% of the 1990 level within 2000, and to reduce the perinatal and neonatal mortality rate by 30-40% within 2000. The strategy aimed at equitable access to care and provision of services at the lowest capable level in the health system. With evidence-based practices, it helped mobilising resources and drew attention to the human rights dimensions of maternal and neonatal mortality. However, the Safe Motherhood Initiative failed to achieve its initial goals, for several reasons. The “risk approach” depended heavily on a health care system that was often neglected or even illusory. Most of the complications of pregnancy and childbirth occurred unexpectedly among the low-risk women, because even though at lower risk, their total number was much higher. This has led to the acknowledgement that all pregnancies should be regarded as “at risk”. Some of the lessons from the Safe Motherhood Initiative were summarised in a meeting in 1997.

An evidence-based strategy, the Mother-Baby Package, was developed by the Safe Motherhood Programme in WHO. The basic main focus of health interventions are family planning, antenatal care, safe delivery, and essential obstetric care. It is being updated as scientific evidence appears.

The International Conference on Population and Development in Cairo in 1994 focused on reproductive rights, particularly the rights of women. Important issues were gender equity, poverty eradication and sustainable development, and access to health care. It also called for
male participation in a key role for bringing about gender equality and responsible parenthood.

**Box 2. The objectives of the Mother-Baby Package**

<table>
<thead>
<tr>
<th>Objective</th>
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<tbody>
<tr>
<td>1. Promote family planning methods</td>
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<td>2. Provide basic maternity care to all women</td>
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<tr>
<td>3. Promote exclusive breastfeeding</td>
</tr>
<tr>
<td>4. Reduce anaemia in pregnancy</td>
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<td>5. Reduce STD in pregnant women</td>
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<td>6. Reduce maternal deaths due to complications of abortions</td>
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<tr>
<td>7. Reduce maternal deaths due to eclampsia</td>
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<tr>
<td>8. Reduce maternal deaths due to hemorrhage</td>
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<tr>
<td>9. Reduce maternal deaths due to obstructed labour</td>
</tr>
<tr>
<td>10. Reduce maternal deaths due to sepsis</td>
</tr>
<tr>
<td>11. Eliminate neonatal tetanus</td>
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<tr>
<td>12. Reduce neonatal deaths due to asphyxia</td>
</tr>
<tr>
<td>13. Reduce neonatal deaths due to hypothermia</td>
</tr>
<tr>
<td>14. Reduce ophtalmia neonatorum</td>
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</tbody>
</table>

Source: WHO

For a long time, antenatal care was a ritual with little scientific (but all the more emotional) justification. Archie Cochrane wrote in 1972; “By some curious chance, antenatal care has escaped the critical assessment to which most screening procedures have been subjected.” A randomised trial comparing the current standard routine antenatal care visits with fewer – but more focused – visits was recently published. The study involved several countries, enrolled more than 10,000 participants in each group, and showed no significant differences in pregnancy outcome for mothers and offspring.

During the last four decades, there has been a remarkable reduction in infant mortality rates, mostly among the post-neonatal infants (1-12 months of age). Recent improvements in infant mortality is largely due to immunization and control of diarrhoeal diseases, whereas stillbirths and neonatal deaths has not decreased at the same rate. The reduced infant mortality rate has been least impressive in Sub-Saharan Africa, and has recently levelled off, partly as a result of the AIDS pandemic (Table 1). However, maternal mortality has not declined in most places, and perinatal mortality is still high. This reflects the difficulties in implementation of the Safe Motherhood interventions, and also the effects of the severe AIDS epidemic. Recent improvements in infant mortality are largely due to immunization and control of diarrhoeal diseases, whereas stillbirths and neonatal deaths have not decreased at the same rate.
### Table 1. Infant mortality rate trends in the world, in deaths per 1000 live births.

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<td>96</td>
<td>79</td>
<td>64</td>
<td>60</td>
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<tr>
<td>Industrialised countries</td>
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<td>20</td>
<td>12</td>
<td>8</td>
<td>6</td>
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<tr>
<td>Developing countries</td>
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<td>108</td>
<td>88</td>
<td>70</td>
<td>66</td>
<td>63</td>
</tr>
<tr>
<td>Sub-Saharan Africa</td>
<td>153</td>
<td>136</td>
<td>119</td>
<td>111</td>
<td>110</td>
<td>108</td>
</tr>
<tr>
<td>Tanzania</td>
<td>142</td>
<td>129</td>
<td>106</td>
<td>102</td>
<td>103</td>
<td>104</td>
</tr>
</tbody>
</table>

Source: UNICEF 16

### 1.2.1 Perinatal and neonatal mortality

The definitions of perinatal and neonatal period is given in Box 3 and illustrated in Figure 1. The older (1977) definition of the International Federation of Gynecology and Obstetrics (FIGO) used 28 weeks of gestations as the start of the perinatal period instead of 22 weeks, and may be more appropriate for low-income countries 17. We therefore used this definition in the current study. Perinatal deaths include stillbirths and early neonatal deaths. The perinatal mortality rate is the number of perinatal deaths divided by the total number of births in the same period. The neonatal mortality rate is the number of neonatal deaths divided by the number of live born babies in the same period.

### Box 3. Definitions of neonatal and perinatal death

**Definitions according to ICD-10, 1992 18**

*The perinatal period commences at the 22 completed weeks (154 days) of gestation (the time when the birth weight is normally 500g), and ends seven completed days after birth.*

*The neonatal period commences at birth and ends 28 completed days after birth. Neonatal deaths (deaths among live births during the first 28 completed days of life) may be subdivided into early neonatal deaths, occurring during the first seven days of life, and late neonatal deaths, occurring after the seventh day but before 28 completed days of life.*

**Definition according to FIGO and WHO, 1977 17:**

*The perinatal period is the one extending from the gestational age at which the fetus gains the weight of 1000 g (equivalent to 28 completed weeks of gestation) to the end of the seventh completed day (168 completed hours) of life.*

*Early neonatal death is death of a live-born infant during the first seven days (168 hours) of life.*

*Late neonatal death is the death of a live-born infant after 7 completed days, but before 28 completed days of life.*
Childbirth is a dangerous event in spite of being a physiological process. The period around birth is a time in life with a very high risk of death, and for all the major causes of neonatal death, the first days of life has the highest risk of death.

**Figure 1.** Illustration of terminology applied to fatal events in the first year of life.

<table>
<thead>
<tr>
<th>Conception</th>
<th>22 wks</th>
<th>28 wks</th>
<th>Birth</th>
<th>7 days</th>
<th>28 days</th>
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<td>Abortion</td>
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<td>Stillbirth</td>
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<td>Perinatal death</td>
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<td>Neonatal death</td>
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<tr>
<td>Postneonatal death</td>
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<tr>
<td>Infant death</td>
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</tbody>
</table>

The World Health Report 2000 estimated that perinatal conditions took 2.4 million lives in 1999, representing 4.2% of the deaths in the world 19. Projections to 2020 have suggested a reduction to 0.9 million deaths 20. Neonatal conditions took almost 4 million lives in 19934, and globally the neonatal and perinatal mortality rate is not decreasing as rapidly as infant mortality.

Most perinatal and neonatal deaths are due to either asphyxia related conditions, immaturity-related conditions, infections, or congenital malformations. Some deaths are directly associated with labour, and may also be the result of poor management of the delivery or a suboptimal health system. Other determinants of perinatal and neonatal deaths are associated with small and preterm babies. Preterm babies have an immature immune system, rendering them more susceptible to infections. They are less capable of enduring the mechanical stress of labour, they are less resistant to hypothermia, and their lungs may be immature. All these factors put preterm babies at a much higher risk of perinatal and neonatal death. The frequency distribution of causes of perinatal death is very different in low-income-countries and high-income-countries. In the high-income countries, the easily treated conditions are rare, whereas malformations and immaturity related conditions predominate. In low-income
settings, the more easily treated conditions like infections and asphyxia related conditions are more commonplace, and may also indicate problems in the health system.

The mother represents the living environment for the foetus, and many maternal factors can lead to small and preterm babies. Systemic infections and urinary tract infections have been associated with preterm delivery and low birth weight \(^{21}\), and so have nutritional deficiencies \(^{22}\) and anaemia \(^{23,24}\). For live-born babies, the death of the mother represents a ‘handicap’ which makes them four to six times more likely to die \(^{25}\).

### 1.2.1.1 Possible interventions to reduce perinatal and neonatal mortality.

No single intervention can prevent perinatal and neonatal deaths. Infant mortality rates have decreased with improving socio-economic development, particularly the postneonatal deaths. Perinatal deaths are more associated with problems during pregnancy and childbirth. Often interventions towards perinatal problems coincide with interventions to improve the maternal health. The quality and access to health services are immensely important. Some evidence-based potential interventions are listed below \(^{5}\).

1. **Before conception:**
   - Increased access and utilization of acceptable family planning methods
   - Supplementation of folate to prevent neural tube defects
   - Management of STDs

2. **During pregnancy:**
   - Improved antenatal care, with detection and management of risk factors and complications like pre-eclampsia, anaemia, malaria, and urinary tract infections (UTI)
   - Tetanus toxoid immunization
   - Improve readiness for delivery and prepare for unexpected complications
   - Practical arrangements regarding delivery place, assistant, where to seek emergency obstetric services in case of serious complications, money and transport, whom to take care of the home in case of complications
   - Involvement of husbands in the preparations, as they are often decision makers and holder of the resources of the household.
3. During delivery:
- the involvement of a skilled birth attendant
- securing clean delivery and avoiding infections of mother and new-born
- detecting complications, particularly bleedings, and being ready to take immediate action

4. Neonatal period:
- rapidly securing respiration and heartbeat of the baby
- avoiding hypothermia
- recommend exclusive breastfeeding
- prevent infections

5. General:
- securing rights and equity for women and children
- improving equitable access to health care that should be culture sensitive
- involve men (often decision makers) to achieve equity and responsible parenthood
- prevention of sexually transmitted diseases (STD) and human immunodeficiency virus (HIV) among both women and men

1.2.2 Anaemia in pregnancy
Anaemia is regarded as a major risk factor for an unfavourable outcome of pregnancy. Severe anaemia is contributing to 5-16% of maternal deaths, and some papers indicate that anaemia in combination with hemorrhage is responsible for 17-46% of maternal deaths. Anaemia in pregnancy has also been associated with low birth weight, preterm birth and perinatal mortality. The association with preterm birth is not firmly established, and the evidence for an association between iron-deficiency anaemia and poor pregnancy outcome may be insufficient. A high Hb is also associated with poor pregnancy outcome. The physiological backgrounds for the adverse outcomes are different for the mother and the child. For the mother, severe anaemia may cause high output cardiac failure, or she may have less blood reserves to withstand hemorrhage during childbirth. For the foetus, maternal anaemia may give a sub-optimal nutritional environment, leading to growth retardation or preterm birth. These again put the child at risk of perinatal and neonatal death. Even though an increased risk of poor pregnancy outcomes among anaemic women might be
very small, anaemia may have a considerable impact when very prevalent. The management of anaemia in pregnancy aims at prevention and treatment of its underlying causes, and is an important part of antenatal service 48.

There is no level of Hb that can confidently define all the anaemic from the non-anaemic persons, since the frequency distribution of Hb in both of these groups overlap considerably. According to the World Health Organization, the definition of anaemia in pregnancy is a hemoglobin concentration (Hb) less than 110 g/l, and severe anaemia if Hb less than 70 g/l (Box 4). Globally, there may be more than 2,000 million people with Hb below the WHO norms 49. It is a particularly common condition among pregnant women, especially in developing countries, where more than half of them may be anaemic 26.

| Box 4. WHO definitions of low hemoglobin (Hb) and hematocrit (Hct) in pregnancy 26. |
|---------------------------------|-----------------|-----------------|
| Anaemia                        | Hb              | Hct             |
| Moderate anaemia               | 70-109 g/l      | 24-34%          |
| Severe anaemia                 | 40-69 g/l       | 13-23%          |
| Very severe anaemia            | < 40 g/l        | <13%            |
| * 105 g/l in second trimester. |                 |                 |

1.2.2.1 Causes of anaemia in pregnancy

Several factors may contribute to anaemia during a pregnancy. The physiological increase in plasma volume is larger than the increase in red cell mass, and leads to hemodilution and decreasing Hb concentration until 7-8 months of gestation. Then Hb increases towards term 50, 51. Hb below 120 g/l is regarded as anaemia in non-pregnant women, whereas among pregnant women Hb below 110 g/l is considered as anaemia (Box 4). Some people use gestational-age-dependent cut-offs for Hb, where the cut-off in 2nd trimester is 105 g/l. The absence of this hemodilution has long been associated with poor pregnancy outcome 31, 38, 46 and hypertensive disorders of pregnancy 37, 47.

The principal pathological conditions leading to anaemia may be related to nutrition, bone marrow suppression, and hemolysis or blood loss.

Iron requirements increase during pregnancy: in addition to the obligatory iron loss (0.2 g), 0.5 g is needed to increase maternal hemoglobin and 0.3 g is needed for the foetus.
Approximately 30 mg is needed for the placenta. The total requirement during pregnancy may be one gram. Iron depletion affects most of the non-supplemented pregnant women, and may lead to anaemia when there is insufficient iron to produce hemoglobin. Iron deficiency is regarded as the most common cause of anaemia in pregnancy worldwide. In a study done in Dar es Salaam, Tanzania, iron deficiency was observed in 86% of anaemic pregnant women.

**Vitamin A** plays an important role in cell growth and differentiation, in addition to the well-known function in the retina. It has also been associated with anaemia, and seems to have additive effect with iron supplementation. During infections, excretion of vitamin A in urine increases and s-vitamin A levels may decrease. The magnitude of vitamin A deficiency in pregnancy in Tanzania was largely unknown at the start of our study.

**Folate** is needed for cell multiplication, and the requirements increase during pregnancy because of increased erythropoiesis and a growing foetus. A typical folate deficiency may lead to megaloblastic anaemia. In addition to its effect on the blood, folate deficiency has been associated with neural tube defects and low birth weight. According to the guidelines for antenatal care clinics (ANC) in Tanzania, folic acid is given free of charge to the pregnant women. This may be good for the women, but is too late at booking to prevent neural crest anomalies. A study from Dar es Salaam found macrocytosis (interpreted as mainly folate deficiency in this setting) in less than 4% of anaemic pregnant women.

**Cobalamin** is usually not considered as a common cause of anaemia in pregnancy, as the body stores are large. Dietary cobalamin deficiency can be seen in strict vegetarians (non-existent in the study area). Insufficient absorption of cobalamin (pernicious anaemia) is usually a disease of older people. This vitamin is involved in the DNA synthesis of cell multiplication, and deficiency can lead to megaloblastic anaemia. Good figures of cobalamin deficiency among Tanzanian pregnant women were not available at the start of this research.

Although single micronutrient deficiencies may cause anaemia, severe anaemia is often caused by several factors acting together. The composition of such a multi-micronutrient supplementation has been suggested, for testing in effectiveness studies. A recent, large study in Nepal showed no better result on birth weight with multi-micronutrients supplementation than with iron and folic acid supplementation.
Aplastic anaemia rarely occurs in pregnancy, but **bone marrow suppression** can occur in systemic infections and malaria \(^{62}\), or as an adverse reaction to drugs (e.g. chloramphenicol).

**Hemolytic** diseases during pregnancy may be genetic (sickle cell disease, thalassaemia, G6PD-deficiency), which are common in certain geographical areas, or acquired (HELLP syndrome). Hemolysis can also be due to malaria infections \(^{63, 64}\). From working in the local hospital, it was evident that patients with sickle cell disease were usually children from the neighbouring district of the study area, whereas among the major ethnic groups of the study area it was rare. The frequency of G6PD deficiency in Tanzania is not well described in the literature.

**Blood loss** in pregnancy may occur as antepartum or postpartum hemorrhage, and may be life threatening within short time. A recent study done in Morogoro, Tanzania, attributed to 17% of maternal deaths to postpartum hemorrhage \(^{65}\).

**Infections** may lead to anaemia in several ways. The inflammation induces a sequestration of iron into the reticulo-endothelial system as storage iron. This may be seen as a physiological response impeding the growth of the invading iron-dependent bacteria, but will also lead to a moderate anaemia because of inhibited (iron-insufficient) erythropoiesis. Infections can also lead to a reduction in red cell survival and bone marrow suppression. HIV infection often produces anaemia, and is quite common in urban areas like Arusha and Dar es Salaam \(^{54}\). The frequency of HIV infection among pregnant women in this area was low, 0.3% \(^{66}\).

**Malaria** infection is the major cause of anaemia among pregnant women in many areas of Africa \(^{54, 67-69}\), and anaemia may develop through several mechanisms \(^{70}\). First, malaria may lead to massive destruction of red cells and hemolysis. Malaria plasmodia invade erythrocytes, mature and multiply through various stages, which in the end lead to bursting of the invaded erythrocytes and the release of new parasites ready to repeat the cycle. Secondly, malaria disease may also suppress the bone marrow and in this way contribute to anaemia \(^{62}\). A third mechanism for malaria to cause anaemia is hyper-splenism. Chronic malaria often leads to enlargement of the spleen, and if the enlargement is gross, hemolysis may be a result of the hyper-active spleen. Malaria may lead to severe anaemia, and if the anaemia develops slowly, Hb values as low as 30 g/l may be observed among women who are walking on foot.
Malaria seems to affect primigravidae more than multigravidae. A study from Zanzibar found signs of malarial infection in 56.5% of primigravidae and 44.7% of multigravidae.

Intestinal parasites are an important cause of anaemia in many developing countries. Persons accommodating blood-sucking hookworms may suffer from considerable occult intestinal blood loss and subsequent anaemia. In a study from Dar es Salaam, it was shown that 44% of severely anaemic and 17% of moderately anaemic pregnant women had intestinal parasites. In the northern highlands of Tanzania, the frequency of intestinal parasitosis was lower than in the coastal areas.

1.2.2.2 Interventions against anaemia in pregnancy
Interventions and tools proven to alleviate anaemia in developing countries, include supplementation of micronutrients, like iron supplementation, folate supplementation, and vitamin A supplementation. Several ways of avoiding the consequences of malaria in pregnancy has been proven effective, like malaria prophylaxis, treatment of presumed malaria with sulphadoxin-pyrimetamin, and use of impregnated bed nets. In a public health perspective, the major obstacles to effective control of anaemia are patient's acceptance and operational constraints.

1.3 THE REPRODUCTIVE HEALTH PROJECT IN MBULU AND HANANG DISTRICTS
The Reproductive Health Project in Mbulu and Hanang districts started as an initiative to study various aspects of pregnancy and childbirth in two rural districts in northern Tanzania, Mbulu and Hanang. Two social anthropologists with background in nursing, were studying cultural aspects in the area, and had shared their concerns with the staff of the local rural hospital, Haydom Lutheran Hospital (HLH), where I was working. As a clinician at the hospital, I had also observed the complications of pregnancy and childbirth, and experienced successes and failures in the management. A colleague with deep roots in the area, Dr. Bjørg Evjen Olsen, was also intrigued by the health problems associated with reproduction and how to improve the outcome of pregnancy. We were challenged to study reproductive health in the area, both mortality and conditions commonly encountered among pregnant women in the area: urinary tract infections, malaria and anaemia. We were both involved in all aspects of the study, and the Centre for International Health, University of Bergen, provided the academic foundation. The existing epidemiological knowledge in the area and the existing
network and facilities at Haydom Lutheran Hospital created a useful site for research activities in the surrounding communities.

A large cohort of antenatal women was selected in order to study the perinatal and neonatal mortality (Papers I and II), and demographic determinants of anaemia (Paper III). Within this cohort, a “nested” case-control study was selected to examine micronutrients and infections as potential determinants of anaemia in pregnancy (paper IV). The maternal hazards of pregnancy in this setting were studied in a collaborating project by Dr. Bjørg Evjen Olsen, focusing on the maternal outcome of pregnancy and on urinary tract infections in pregnancy 83-87.
2 Aims and objectives

The current study is part of a larger study of maternal and child health in the area. Previously a PhD thesis entitled “Motherhood – A hazardous endeavour” described findings related to maternal death, and to urinary tract infections. The current study is primarily based on the same population.

Aims
The aim of the project was to study the outcome of pregnancy. We wanted to study known and potential determinants of perinatal and neonatal mortality in the area, and in particular anaemia in pregnancy. The project intended to provide a basis for measures to improve the health of mothers and children.

Objectives
The specific objectives of the study were to:

1. Estimate the perinatal mortality rate in Mbulu and Hanang districts.
2. Study known and potential determinants of perinatal deaths in Mbulu and Hanang, including anaemia, malaria, and urinary tract infections.
3. Study the causes of stillbirths and neonatal deaths in Mbulu and Hanang districts.
4. Study the avoidability of stillbirths and neonatal deaths in Mbulu and Hanang.
5. Study the prevalence of anaemia in pregnancy in Mbulu and Hanang districts in Tanzania.
6. Study known and potential determinants of anaemia in pregnancy.
7. Study the associations between anaemia and iron-status, folate status, cobalamin status and vitamin A status.
3 Description of study area

3.1 TANZANIA

Tanzania had a long history as a colony, first under German rule (1884-1920), then British (1920-1961), before it became independent in 1961. In 1964, Tanganyika united with Zanzibar to form the United Republic of Tanzania. Many Sub-Saharan African countries have been marred with civil war, but Tanzania has been remarkably peaceful in this regard. The Arusha declaration of 1967 stated the “villagization” policy, an African socialism based on collective agricultural venture running along traditional African lines. It aimed at self-reliance and providing essential services to the people, notably education but also health services. The economic policy failed to develop according to the expectations. Approximately 60% of the population have less than 2USD a day, and survive by agriculture. A poverty reduction policy is being implemented with the assistance of the World Bank. In 1995 the first multi-party election took place. Still, the ruling party Chama cha mapinduzi (CCM, Swahili: “Revolution party”) got 60% of the votes and won, reflecting the deep-rooted extensive influence of the party.

Tanzania (map p.16) is a large country in East Africa covering 945,000 km², almost twice as large as France. According to the census in 2002, the population is approximately 34 million, and the population growth rate is 2.9%. The World Health Report 2001 indicates that half of the population is below 15 years of age, and only 4% are over 60 years. The infant mortality rate is estimated to be 85 per 1000 live births, and life expectancy at birth is 45 years. Most of the population live in rural areas (67%), and 56% have access to an improved water source. 24% of the population over 15 years are illiterate. There are more than 120 ethnic groups with different languages, but most people speak the official language Swahili, and many speak English, the second official language. According to official figures, agricultural export, including coffee, cotton, tea, tobacco, cashewnuts and sisal, accounted for 56% of merchandise exports (1996-99). Minerals also represent major export revenues, and are growing. The booming tourist industry relying on the extraordinary wildlife environment in Tanzania, creates ten times as great revenue as the minerals.
3.1.1 Health system in Tanzania

The health expenditure in the years 1992-98 was 3% of GDP, divided between public (1.3%) and private (1.8%) \(^{93}\). This amounts to 8 USD per capita (15 USD purchasing power parity, PPP). The health service structure is governed by the Ministry of Health in Tanzania, but the services are provided by government, voluntary agencies, and private companies. The health “pyramid” consists of several levels of care. According to the Ministry of Health figures, in the year 2000 there were more than 5000 village health workers, approximately 3500 dispensaries, 480 health centres, and 180 hospitals \(^{88}\).

The Village Health Service is the lowest level of health care delivery in the country. They essentially provide preventive services that can be offered in homes. Usually, each village health post has two village health workers chosen by the village government amongst the villagers and given a short training. The dispensary services represent the second level in the health services pyramid. A dispensary caters for 6,000 to 10,000 people and supervises all the village health posts in its ward. There were approximately 4000 registered dispensaries in Tanzania (approximately 2500 government owned). A dispensary may be staffed by a nurse/midwife and a rural medical aide, and usually has a labour room and provide essential obstetric services. A Health Centre is expected to cater for 50,000 people, which is approximately the population of one administrative division (tarafa). There were about 500 registered health centres in Tanzania (400 owned by government). Health centres are staffed by Clinical Officers, Nurses and Midwives. The health centre usually has beds and delivery facilities, including vacuum extraction and intravenous infusion, but not blood transfusion and surgical facilities. Each district is supposed to have a district hospital (DH), headed by the District Medical Officer, who is an assistant medical officer or a medical doctor by training. In some districts, a voluntary agency hospital is designated to be a district hospital (DDH), and get subventions from the Government to contract terms. In 2000, there were 55 government DH, 13 DDH, and 86 other hospitals in Tanzania; the HLH in the study area is one of latter. The 17 Regional Hospitals in Tanzania offer similar services like the district hospitals, but in addition give specialist services that are not provided at district hospitals. The four Consultant Hospitals constitute the top of the health pyramid, and are large teaching hospitals with specialist services \(^{88, 94}\).

Non-profit voluntary agencies play an important role in the institutional health services in Tanzania, representing more than 50% of the hospitals, including some teaching hospitals and
a university hospital. The largest contributors are the Catholic Church, the Evangelical Lutheran Church, and the Anglican Church. All the hospitals receive staff- and bed-grant from the government, underscoring their place in the health system, and they report to the Ministry of Health through the appropriate channels. These voluntary agencies were organised in a body called Christian Social Services Commission (CSSC), negotiating with the donors and the government.

In line with the economic reforms advocated by the World Bank and IMF, the health sector is currently undergoing reforms (HSR). The aim is to improve the performance of the health sector, by emphasising efficiency, equity and quality of the services. The strategies are decentralization, program integration, self contributions, focus on essential services packages, sector-wide approaches, civil service reform, insurance coverage, and engaging the private sector.

One of the problems in many sectors in Tanzania is low motivation that may be related low salaries. Often a medical doctor can earn more money in business than by working as a doctor. There is a shortage of medical doctors in rural Tanzania. Understandably, the cities provide more opportunities for them, and many Tanzanian doctors have moved abroad to neighbouring countries. A system of meriting at rural posts may improve coverage.

3.2 MBULU AND HANANG DISTRICTS AND THE STUDY AREA

The study was conducted in Dongobesh division of Mbulu district, and Basotu division of Hanang districts in the northern part of Tanzania, in Arusha region 200 km south of the famous Ngorongoro crater. The Great Rift Valley cuts through the area, giving rise to a varied topography. Most of the area lies on a plateau 1600-2200 meters above sea level, while the Yaeda valley is at approximately 1300 m. The highest areas have rainforest. Most of the uninhabited area is covered with savannah grass, bushes, and acacia trees. The extinct volcano Mt. Hanang (3390m) is among the highest mountains in Tanzania and a landmark in the study area. The climate is temperate, with mean temperature between 20-30 ºC. During the dry season, there is usually no rain. There is usually a short prelude of rains in November-December, and the long rains usually lasts from January till May (Fig.2). The average annual rainfall is 600-800 mm. According to MARA map, the climate is suitable for hypo- and meso-endemic malaria transmission.
3.2.1 Infrastructure

The infrastructure is not strong in the area. There are no tarmac roads, and the dirt roads may be difficult to pass in the rainy season. The main roads are maintained by the district council when the budget allows, and feeder roads in the study area are constructed by the Haydom Lutheran Hospital with technical support from the district. The collaboration came as an initiative from the hospital to improve access and availability of patient transport, and is supported by external donors. The rainy season often creates problems of transport because of mud and erosion.

Several bus services exist, linking Haydom town with Mbulu, Arusha, Katesh and Singida. The buses depart once daily, and schedules are unpredictable. Few people in the study area have a vehicle, but cars exist in Haydom, Dongobesh, and Basotu. A bicycle is widely used by men, while only a few women use one. Transport of pregnant women to clinics and to hospital is often on the carrier of a bicycle. Walking is the most common way of travelling.

In the study area, there were no telephone lines in 1995, and few houses and institutions had power via the national electricity network. The closest telephone was in Mbulu town at that time. However, very-high-frequency (VHF) radio contact exists, linking distant villages together with Mbulu town and with the HLH. Most of the VHF radios are owned by the HLH and placed in the houses of entrusted persons. If the operator is temporarily away, another person in the house will operate it. The radios are robust and running on solar panel-charged
batteries. The radios provide communication facilities for villagers to call the ambulance at the hospital. The radio is available day and night at the HLH. Recently, telephones have become more common.

### 3.2.2 Cultural characteristics

According to the 1988 census and a growth rate of 3.8%, Basotu and Dongobesh divisions (the study area) had approximately 143,000 inhabitants in 1995 during the data collection. Most of the people in the study area belong to the ethnic groups of Iraqw and Datoga. Two socio-anthropologists, Ole Bjørn Rekdal and Astrid Blystad have studied their culture, and many issues are depicted from their work 79-82, 97-103.

These two ethnic groups have different origins. The Iraqw are speaking a Cushitic language, whereas the Datoga belong to the Nilotic-speaking group (like the Masai). There is extensive intermarriage between the two ethnic groups, and the real identity is often ambiguous. Some Datoga would state they are Datoga in one situation and Iraqw in another situation 99. Some names are similar as well. The leather skirt of women is often the best way of identifying women living in a traditional Datoga way. The Iraqw are agropastoralists, and the Datoga originally pastoralists, but are more and more adapting to agriculture. For both ethnic groups, the main commodity of wealth is cattle. In a household survey conducted in the study area, the number of cows in a household was reported to be 7-8 cows for both ethnic groups. Less than 2% of the households had more than 30 cows, and 15% had no cattle. 10% had an acre of field or less, and less than 3% of households had more than 10 acres of field. Average acreage was between 3 and 4 acres per household. However, all these numbers are according to their own statements, which are always somewhat underreporting.

In addition to the Iraqw and the Datoga, other ethnic groups exist in smaller numbers, notably the Iramba and Nyaturu who dominate in the Singida District south of the study area. There is very limited intermarriage between these ethnic groups and the Iraqw and the Datoga. A few other groups are also scarcely represented (Chagga, Pare), often being civil servants or business people from other parts of the country.

There is considerable cultural overlap between the two major ethnic groups in the area, the Iraqw and the Datoga. However, a higher proportion of Datoga live in a "traditional" way,
whereas more Iraqw adapt to a more "modern" village life. There is for example a highly visible manifestation of traditional culture among datoga, including female dress and decoration. Such aspects of "traditional" culture are to a considerable degree stigmatized among the ones who have moved towards a more "modern" way of life. This fact may influence the extent to which datoga women attend the antenatal clinics, and could therefore introduce some selection bias.

Procreation is a central matter in both ethnic groups, and both are traditionally polygamous. Having children is associated with status, security, creation of a workforce, and the meaning of life itself, resulting in a commitment to family growth. A man without offspring is often disregarded, and even his funeral may not be honoured properly. Childless women may get both emotional and social stress, and may end up in divorce. Infertility has a very strong stigma, and is used as a derogatory and offensive term. Concepts of "stuck pregnancies" are common, and may indicate several medical conditions, such as early spontaneous abortions, missed abortions, and irregular menstruation. After such events, a woman may still regard herself as pregnant, but the foetus "went back". Later, it may start growing again "spontaneously" and some women may therefore state a pregnancy duration of 10 years.

The purpose of modern family planning is often not well accepted. It is often misunderstood or not understood at all, as a high number of children is not a threat, but is regarded as a blessing. Not the least due to the cost of living, some people are beginning to use modern family planning devices, particularly injections.

The Datoga are intensely preoccupied with the protection of fertility. Successful birth giving is not taken for granted, and pregnancy and infancy are often protected by many complicated customs. The pregnant woman will try to avoid conflicts with anybody in the household, including the husband. A husband's beating of his pregnant wife is unacceptable, unlike for non-pregnant women. It is regarded as a sin against fertility and womanhood at large, and may result in penalty or even a curse or excommunication if he is remorseless. The pregnant woman should avoid rivers and lakes, the dwelling place of evil spirits. She must also be careful with strangers, as they may have a bad influence on the foetus, and therefore large crowds of people should be avoided. This could certainly be a problem for antenatal attendance, which fortunately seems to be increasingly accepted. During pregnancy, the woman is often given the food she craves for. This may include very nutritious food such
as blood, liver and kidneys. There is no custom of starving the pregnant women in the third trimester, like the Masai women sometimes do. The delivery is usually assisted by the mother-in-law, and is associated with many religious concepts. If mucus obstructs the nose and mouth, the attendant may suck the face of the newborn after delivery. However, the colostrum is regarded as impure, and the infant is often given water the first few days until there is no meconium left. Thereafter the mother usually lets the child exclusively breastfeed for 3-4 months. She may continue with some breastfeeding until the age two years. This is also reflected in obstetric histories of women in the area, where two years is the most common interval between children. After delivery, the mother is usually not allowed to move freely outdoors, and she is fed well. Still, a visit to a clinic for assessment and vaccination of a child is often accepted when the baby is a month.

A unique custom among the Iraqw, and the also the Datoga, is their seclusion practices, *meeta* and *metid*. It involves temporary cultural consequences of fertility related events like the death of the child, the death of a mother, and the pregnancy of unmarried girls. Persons under *meeta* are excluded from normal social life and live separated from others. The household of a woman who loses a lactating child or has a still birth or an abortion, is in *meeta*. It usually lasts until the woman is pregnant again. Also, the house of a family where a pregnant or delivering or lactating woman dies, is considered to be in *meeta*. This practice may have an impact the completeness on follow-up in our study, and to some extent on the interviews with the deceased.

With the strong religious sentiment associated with pregnancy and childbirth, the adoption of antenatal services and modern obstetric care is not without reservations. Often we find traditional Datoga women rather sceptical, though not rejecting services altogether. The Iraqw have a tradition of employing foreign healers, which may be part of the reason why they accept more easily both antenatal clinics and modern obstetric care. Probably this has introduced some bias towards a higher proportion of Iraqw women in the antenatal cohort compared to the general population in the area. For utilization of hospital delivery services, the bias is probably stronger.

The staple food in the area is maize, usually eaten as porridge ("ugali") with green vegetables or with beans. Meat from chicken and goats is commonly used, while beef is used mostly at celebrations. Pigs exist in some “modern” households, but are regarded as unclean by the
Datoga. All parts of the animals are used for food. Many households extract oil from sunflower. General famine is uncommon, but the area experienced a draught in 1999-2001, with below average rainfall and meagre crops. According to the previously mentioned household survey in the area, less than 4% had safe drinking water next to their homes. Only 28% had safe water within an hour’s walking distance from home, the remaining households had longer distances. A household had on average 6.3 persons, and among the persons in these rural villages, 60% of the men and 40% of the women are literate.

3.2.3 The health services in the study area.

In the study area, there is one hospital, one health centre and 15 dispensaries, all presumably providing Basic Obstetric Care 107 (map of study area p.25). Only Haydom Lutheran Hospital (HLH) provides surgical services and Comprehensive Obstetric Care in the study area. Outside the study area there are hospitals in Mbulu (80 km from HLH) and in Dareda (110 km from HLH) offering Comprehensive Obstetric Care. In 1995 there was one health centre in Dongobesh and 14 dispensaries in the study area. Many of the dispensaries regularly assist deliveries, but they are often short of equipment. The study was conducted based at the HLH.

The District Medical Officer (DMO) in the district headquarters is the leader of health services in the district. All health facilities in the district report to him. The "Mother-and-child-health" (MCH) work is of the cornerstones in the primary health care, with an MCH co-ordinator stationed at the district hospital under the DMO, supervising and supplying vaccines and equipment. The MCH work is usually an integrated part of any health institution. MCH clinics offer antenatal examinations and counselling, child assessments, vaccinations, family planning and health education. Women or children with diseases or at risk of diseases are supposed to be referred to a higher level of care, i.e. a clinic or a hospital. Some institutions run outreach clinics in order to come closer to the users. An MCH team from the HLH visits the outreach clinics once monthly, usually taking place in a church or a government building.
Map of study area
In 1995, 1% of the budget of Mbulu district was spent on health, and 37% was spent on providing safe water sources (sponsored by donors)\textsuperscript{108}. Sanitation is one of the tasks of the village health workers, and digging pit latrines was enforced by law. Pit latrines are becoming more and more commonplace, although not everybody has one. In the household survey we found that only 20-30% of the households had a latrine.

The largest health institution in the area is HLH, where the study was based. Annually, the HLH has approximately 60,000 outpatients and 10,000 admissions. The hospital runs an extensive MCH work, with one clinic at the hospital and 12 (1995) outreach clinics in remote areas to ease the access to maternity care for women living far away. An ambulance system exists at the hospital, with two vehicles collecting more than a thousand patients a year\textsuperscript{109}. The payment for the transport is added to the total hospital bill, which prevents rejection of patients who have no cash immediately available. Maternity cases have priority, and represent a quarter of all the users. The users can request the ambulance directly at the HLH, or via the VHF-radio stations in the area.

3.2.4 Health and disease in the study area

The disease pattern in the study area is reflected in the statistics of the HLH from 1995 (Tables 2 and 3). Malaria is the most common ailment causing people to seek health services, and it is also the most common cause of death. Problems of the newborn also rank high on the list of cause of death.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{perinatal_mortality.png}
\caption{Perinatal mortality rate at Haydom Lutheran Hospital 1992-99.}
\end{figure}
In 1995, there were 2190 deliveries at the hospital, 55 with twins and a triplet; 202 (9%) of the deliveries were done by a caesarean section. The maternal mortality ratio (MMR) in the area was recently estimated to be 300-400/100,000 \(^{84-86}\). The main cause of maternal mortality was cerebral malaria \(^{86}\). The perinatal mortality rate at the hospital is approximately 50/1000 births (Fig.3).

Table 2. The most common causes of death among hospital admissions at the Haydom Lutheran Hospital, 1995 \(^{110}\).

<table>
<thead>
<tr>
<th>Rank</th>
<th>Diagnosis</th>
<th>Hospital deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Malaria</td>
<td>357</td>
</tr>
<tr>
<td>2</td>
<td>TB</td>
<td>111</td>
</tr>
<tr>
<td>3</td>
<td>Prematurity</td>
<td>62</td>
</tr>
<tr>
<td>4</td>
<td>Pneumonia</td>
<td>49</td>
</tr>
<tr>
<td>5</td>
<td>Heart disease</td>
<td>36</td>
</tr>
<tr>
<td>6</td>
<td>Malignancy</td>
<td>25</td>
</tr>
<tr>
<td>7</td>
<td>Birth asphyxia</td>
<td>19</td>
</tr>
<tr>
<td>7</td>
<td>Diarrhoea</td>
<td>19</td>
</tr>
<tr>
<td>9</td>
<td>Meningitis</td>
<td>17</td>
</tr>
<tr>
<td>10</td>
<td>Malnutrition</td>
<td>14</td>
</tr>
<tr>
<td>11</td>
<td>HIV / AIDS</td>
<td>13</td>
</tr>
</tbody>
</table>

The deaths in the table represented 85% of the deaths at the hospital.

Table 3. The most common diseases diagnosed at the outpatient department of the Haydom Lutheran Hospital, 1995, Tanzania \(^{110}\).

<table>
<thead>
<tr>
<th>Rank</th>
<th>Disease</th>
<th>Outpatient cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Malaria</td>
<td>19811</td>
</tr>
<tr>
<td>2</td>
<td>Pneumonia</td>
<td>3824</td>
</tr>
<tr>
<td>3</td>
<td>Amoebiasis</td>
<td>2433</td>
</tr>
<tr>
<td>4</td>
<td>Bronchitis</td>
<td>2124</td>
</tr>
<tr>
<td>5</td>
<td>Eye diseases</td>
<td>1808</td>
</tr>
<tr>
<td>6</td>
<td>Giardiasis</td>
<td>1807</td>
</tr>
<tr>
<td>7</td>
<td>Animal/insect bites</td>
<td>1747</td>
</tr>
<tr>
<td>7</td>
<td>Ear diseases</td>
<td>1497</td>
</tr>
<tr>
<td>9</td>
<td>Sore throat</td>
<td>1329</td>
</tr>
<tr>
<td>10</td>
<td>Gastro-enteritis</td>
<td>1269</td>
</tr>
</tbody>
</table>

Evident from the hospital statistics, one of the major health problems is malaria, both with respect to morbidity and mortality. The area has a climate suitable for meso-endemic transmission. There are many malaria cases throughout the year, but the incidence increases during the rainy seasons, and all age groups are affected. According to hospital data of 1995, the Case Fatality Rate of cerebral malaria was approximately 30% for both children and adults. In addition to the annual increase in malaria incidence during the rainy season, epidemics are also seen when the annual incidence cycle is much larger than expected. The year of the field study was such an epidemic year (Fig.4).
The raging HIV epidemic in Tanzania with an estimated 1.5 million infected in 2002\textsuperscript{111}, had not yet struck this area as hard as many other parts of Tanzania in 1995. The prevalence of HIV sero-positives among consecutive ANC attendees tested anonymously was 0.3\% in 1996 and 0.4\% in 1999\textsuperscript{66}. In 2001, there was a rise in the proportion of HIV sero-positives among blood donors (Fig.5).

Alcohol abuse and its adverse social consequences are becoming more common\textsuperscript{97, 108, 112}. It may seriously have influenced the health seeking behaviour of patients and important decisions during pregnancy and childbirth.

A study of maternal morbidity and mortality in the area has recently been completed in a collaborating project\textsuperscript{83-87}. It used mostly the same study subjects as this study.

The maternal mortality ratio (MMR) was estimated by using the “sisterhood” method\textsuperscript{84}. The respondents’ family histories were the basis for the calculations, namely, how many of the respondents’ sisters died during pregnancy, delivery or shortly thereafter. It estimates the
MMR approximately 10 years prior to the survey. The MMR was estimated to be 362/100000 live births among women who attended the antenatal clinics in the area, and 444/100000 in the household study. This was lower than what has been found in other areas of Tanzania. Increasing distance of the ANC clinic to the hospital was associated with a higher MMR.

The maternal mortality ratio (MMR) was also estimated in other ways in the area. In 1995 and 1996, 45 maternal deaths were found in the study area, using multiple sources. The MMR was estimated to be 388 (95% CI 250-560) per 100000 live births (using multiple sources), 322 (95% CI 160-580) per 100000 live births in the antenatal cohort, and 123 (95% CI 70-200) per 100000 live births using official statistics. There was a severe underreporting from official statistics and health institutions.

The maternal deaths (n=45) that occurred in the study area during 1995-6 were traced, evaluated and analysed. Indirect obstetric deaths (n=32, 71%) were more common than direct obstetric deaths (n=13, 29%) in this setting. The main cause of direct maternal deaths was hemorrhage, while among indirect causes, malaria predominated (n=20). The majority of the women died at a health facility (41 of 45), and 24 of the 45 women died postpartum. Only 11 of the pregnancies (24%) resulted in children who were alive at follow-up. Approximately 30% of the deaths were considered avoidable under the prevailing circumstances. The reasons were particularly delay in seeking help and failure of family to recognize the severity of the condition.

The cohort of pregnant women was also examined for urinary tract infections (UTI). Various examinations were done to detect different aspects of a UTI. The dipstick test for nitrite in urine for detecting bacterial activity was positive in 40%, whereas leukocyte esterase test showing leukocyte activity in urine was positive in 65%. A simple question about dysuria was positive in 32% of women. Bacterial culture using the Uricult® dipstick was positive in 16%. The prevalence of UTI was significantly higher in the rainy season for all the tests. The correspondence between the tests was poor.
4 Subjects and methods

4.1 SELECTION OF SUBJECTS

There were two sources of study subjects: one from a follow-up study at the MCH clinics run by HLH, and one from a simultaneous household survey. Our main source of subjects was the MCH clinics, where the research was done concurrently with the regular work. There were 12 antenatal clinics in the study area operated by the HLH, and the women attending these clinics

Figure 6. Outline of the study populations and selection procedures.
SB = stillborn; END = early neonatal death; LND = late neonatal deaths.
constituted our study population in this paper. We hired five field assistants to help collect the data at the MCH clinics, by recording results, examining the blood and urine, and conducting interviews. Usually two stayed at the MCH department of the hospital and three were going on outreach visits with the “mobile” MCH team. The field assistants were trained, and supervised throughout the data collection period.

The household survey covered 7 of the 183 sub-villages (vitongoji) in the study area, a total of 1282 households. The head of household was interviewed by a research assistant, and a woman of the house was interviewed by another research assistant. Only 12 households were missing and 11 refused to be interviewed.

Figure 6 shows the selection procedure of the study population. The antenatal clinic attending women were 5239, of whom 767 were living outside the study area. Of the remaining 4472 women, 3836 were examined for anaemia and constituted the study population for paper III. At four of the clinics, with 2547 attending women, we selected 312 women for a nested case-control study with serological investigations (Paper IV).

Among the 4472 attending women living in the study area, most of them were registered at the HLH clinics. However, some of the attendants (777) had registered at another clinic previously and were not included for follow-up. Some women later proved not to be pregnant and were excluded (71). A few (6) were excluded for other reasons. The remaining 3618 women, where we had full information and address, were followed up to assess the outcome of pregnancy (Paper I). We got information on the pregnancy from 3512 of them.

From the household study we identified 370 births that had occurred the previous year. Of them 6 were still births, 8 were early neonatal deaths, and 7 were late neonatal deaths. These were included in the case series together with cases from the cohort, as described in Paper II.

4.2 STUDY DESIGN

4.2.1 Paper I: Perinatal mortality.

Paper I is a follow up study of 3618 consecutive antenatal visitors who were registered at the antenatal clinic of HLH. The perinatal mortality rate and its determinants were assessed. Women attending the ANC clinics and who were living in Dongobesh and Basotu divisions
were included in a cohort and were followed up after delivery. The follow up of the attendees was done on the first visit after delivery, when the mother brought her new child for vaccination. The women who did not come back to the clinics, were traced back to their home village, and inquired about the condition of the mother and the child. Perinatal deaths include stillborn babies and early neonatal deaths. The perinatal mortality rate of a population is the number of deaths occurring during the perinatal period per 1000 births, and therefore including stillbirths in the denominator. This contrasts the definition of neonatal mortality rate, defined as the number of neonatal deaths per 1000 live births.

The outcome measures of this paper were the perinatal mortality rates and the risk of perinatal deaths. The determinants studied were parity, previous loss of child, previous miscarriage, birth weight, maternal urine nitrite, maternal anaemia, maternal malaria, maternal VDRL serology (Venereal Diseases Research Laboratory examination, unspecific syphilis test), and maternal arm circumference. The information on some determinants was incomplete in parts of the cohort.

4.2.2 Paper II: Avoidable stillbirths and neonatal deaths.

Paper II is a review of all the stillbirths and neonatal deaths that occurred in our cohort of 3618 pregnant women. In addition to the 53 still born and 42 early neonatal deaths described in paper I, we included the 16 late neonatal deaths from the same cohort. In order not to miss important causes of death among women who did not attend antenatal clinics, we also included women from the household survey who had lost a neonatal baby or had a still birth. There had been 370 births during the last 12 months prior to the household visits, 6 were still births, 8 died during early neonatal period and 6 died during late neonatal period.

The women in this case series who lost a neonatal baby or had a still birth, were identified, interviewed, and the cause of death was suggested. Three doctors independently evaluated the record of each case and reached a diagnosis, and where at least 2 doctors agreed, we kept the diagnosis. If all doctors had set a different diagnosis, we discussed the case and reached consensus. The cases were reviewed and commented upon by a paediatrician, whereupon we re-evaluated the diagnoses to reach consensus. For each case, we also assessed the avoidability of the death, whether patient-oriented or service provider-oriented. There are several ways of defining avoidable deaths. We defined a death as avoidable if there was a
preventable factor that likely contributed to death, under the ruling circumstances. We judged various degrees of likelihood for avoidability, and thus death would probably or possibly be averted if the factor was removed. We also assessed whether antenatal risk factors were present, and whether the mother of the deceased knew that she had a risk factor.

4.2.3 Paper III: Anaemia in pregnancy.

The women in the cohort were also examined for Hb and analysed cross-sectionally for (mostly) demographic determinants of anaemia (Paper III). We recorded 5239 attending women during the study period, and offered them Hb examination in addition to the ordinary antenatal routine investigation. Women who came from villages outside the study area were excluded from the analyses, and some women who later proved to be not pregnant, were also excluded. We included 3836 women to evaluate determinants of anaemia cross-sectionally.

The outcome measures of this study were Hb and the proportion of anaemic women (or “frequency of anaemia”), and we calculated the odds ratio (“risk”) of anaemia. For analytical purposes, we defined three groups according to their Hb: one non-anaemic group with Hb ≥ 110 g/l as reference, one group with moderate anaemia with Hb 90-109 g/l, and one group with more pronounced anaemia with Hb < 90 g/l. The main determinants studied were maternal age, altitude of residence, ethnic group, religion, duration of pregnancy, parity, season, and malaria parasitaemia.

4.2.4 Paper IV: Determinants of anaemia in pregnancy.

We also wanted to examine the role of nutritional factors and infections as determinants of anaemia in pregnant women. Therefore we selected, according to their Hb results, some of the women in the cross sectional study into a “nested” case-control study. We selected 312 out of the 2547 screened attendants at 4 of the 12 antenatal clinics of the cohort in paper I. In order to have representative sample from different Hb levels, we chose a nested case-control study design (for details see Paper III). We analysed the groups Hb ≥ 110 (n=153), Hb 90-110 (n=89), Hb < 90 (n=70). We selected simultaneously from two clinics, and therefore the numbers were not equal in each stratum. The selected subjects were interviewed and gave venous blood for further examination.
The outcome measures were defined as the risk of having anaemia with Hb below 90 g/l, and the risk of having anaemia with Hb 110-90 g/l. As determinants we examined both micronutrients and some markers of infections, and other characteristics: s-ferritin, s-Fe, s-TIBC, s-folate, s-cobalamin, s-vitamin A, s-C-reactive protein (CRP), s-lactate dehydrogenase (LD), s-haptoglobin, malaria blood slide, urine nitrite positive, and arm circumference.

### 4.2.5 Study power

The various parts of the study had various statistical powers to detect associations depending on the number of women included and the prevalence of the conditions being studied. Papers I, II, and III were based on the available data from a cohort of all ANC clinic attending women for about a year. The size of the cohort was determined by the attendance of pregnant women and the available time frame for data collection.

```
Table 5. Study power (1-β) to detect associations between determinants and anaemia (Hb < 90 g/l), according to the odds ratio of the determinants.

<table>
<thead>
<tr>
<th>OR</th>
<th>Study power (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5 %</td>
</tr>
<tr>
<td>1.5</td>
<td>11.9</td>
</tr>
<tr>
<td>2</td>
<td>30.3</td>
</tr>
<tr>
<td>3</td>
<td>71.7</td>
</tr>
<tr>
<td>5</td>
<td>98.5</td>
</tr>
</tbody>
</table>
```

Paper IV was based on a case-control study “nested” within the cohort. Altogether 312 women with various levels of Hb had been included to facilitate comparisons of both pronounced (Hb < 90 g/l) and mild (Hb 90-109 g/l) anaemia with normal controls (Hb ≥ 110 g/l). The power (1-β) in paper IV to detect associations between pronounced anaemia and the determinants are given in the Table 5. Among controls, the prevalence of most of the
exposures of determinants was 15-50%. Evident from Table 5, an odds ratio (OR) of 1.5 was difficult to detect even for prevalent exposures. An OR of 3 or more was, however, likely to be detected. A determinant with an OR 2 would likely be detected for risk factors with high prevalence among controls.

4.3 LABORATORY METHODS

For examination of hemoglobin concentration, we used two HemoCue® devices measuring capillary blood, one for the MCH clinic at the hospital, the other for the outreach (“mobile”) clinics. Thick blood slides were prepared according to the routines at HLH, using capillary blood and Field staining. The number of plasmodia per 100 white blood cells was recorded. In negative slides, at least 20 fields were examined before stating negative, which is lower than what is recommended 113. This could increase the number of false negative slides, but not influence the positives. It could partly explain why malaria slide is not very closely associated with anaemia, but blood-slide negative malaria is a very well-known clinical problem in the area. A mid-stream urine sample was obtained from the women, and a Uricult® dipslide culture of the urine was done, incubated for 18-24 hours at 37°C and then recorded. A Nephur6® dipstick test was also done, giving instant result of nitrite, leukocyte esterase, glucose, albumin, and blood in the urine. Reading of results was done after a minute, according to manufacturer's instructions.

Women selected for a study on anaemia, were venipunctured with a Vacutainer® system. The blood was left for 30 minutes to clot, centrifuged and the serum was then pipetted into sterile tubes. The sera were frozen at -21°C. The sera melted once due to electricity failure. The frozen sera were brought to Laboratory for Clinical Biochemistry at Haukeland University Hospital in Bergen by air. Then the sera were analysed for vitamin A, iron status, folate, cobalamin, CRP, LD, haptoglobin, creatinin, and vitamin E. Some of the sera had insufficient quality for CRP and haptoglobin analyses. In our analyses, we used the definitions of abnormal values given in Table 6.
Table 6. Abnormal values for laboratory methods used.
Most of them depicted from manual of the laboratory.\textsuperscript{114}

<table>
<thead>
<tr>
<th>Analysis</th>
<th>Abnormal values</th>
<th>Method/Equipment</th>
</tr>
</thead>
<tbody>
<tr>
<td>B-hemoglobin (Hb)</td>
<td></td>
<td>HemoCue B-Hemoglobin, HemoCue</td>
</tr>
<tr>
<td></td>
<td>&lt; 110 g/l*</td>
<td>WHO definition for anaemia in pregnancy.</td>
</tr>
<tr>
<td></td>
<td>&lt; 90 g/l**</td>
<td>Used in analyses in Paper III and IV</td>
</tr>
<tr>
<td></td>
<td>&lt; 70 g/l***</td>
<td>WHO definition of severe anaemia</td>
</tr>
<tr>
<td>S-cobalamin</td>
<td>&lt; 150 pmol/l</td>
<td>MSA, Technicon Immuno-1, Bayer Corp.</td>
</tr>
<tr>
<td>S-C-reactive protein (CRP)</td>
<td>&lt; 10 mg/l</td>
<td>Immunoturbidometric, Orion Diagnostics.</td>
</tr>
<tr>
<td>S-ferritin</td>
<td>&lt; 15 µg/l</td>
<td>MSA, Technicon Immuno-1, Bayer Corp.</td>
</tr>
<tr>
<td></td>
<td>&lt; 50 µg/l*</td>
<td>* if CRP &gt; 10 mg/l,\textsuperscript{115}</td>
</tr>
<tr>
<td></td>
<td>&gt; 75 µg/l**</td>
<td>** 97.5 percentile of non-anaemic women in the study</td>
</tr>
<tr>
<td>S-folate</td>
<td>&lt; 4.5 nmol/l</td>
<td>MSA, Technicon Immuno-1, Bayer Corp.</td>
</tr>
<tr>
<td>S-haptoglobin</td>
<td>&lt; 0.4 g/l</td>
<td>Behring Nephelometer Analyser II, Dade Behring.</td>
</tr>
<tr>
<td>S-iron</td>
<td>&lt; 11 µmol/l</td>
<td>Spectrophotometer, Technicon Chem-1, Bayer Corp.</td>
</tr>
<tr>
<td>S-lactate dehydrogenase (LD)</td>
<td>&gt; 450 U/l</td>
<td>Spectrophotometer, Technicon Chem-1, Bayer Corp.</td>
</tr>
<tr>
<td>S-TIBC</td>
<td>&gt; 72 µmol/l</td>
<td>Spectrophotometer, Technicon Chem-1, Bayer Corp.</td>
</tr>
<tr>
<td>S-transferrin saturation</td>
<td>&lt; 16%</td>
<td>Calculated by formula: Tfsat= (100 x Fe/TIBC) %</td>
</tr>
<tr>
<td>S-vitamin A</td>
<td>&lt; 0.7 mmol/l</td>
<td>High performance liquid chromatography.</td>
</tr>
<tr>
<td>Urine leukocyte esterase</td>
<td>+, ++, +++</td>
<td>Nephur 6, Boehringer-Mannheim.</td>
</tr>
<tr>
<td>Urine nitrite</td>
<td>(+) and +</td>
<td>Nephur 6, Boehringer-Mannheim.</td>
</tr>
</tbody>
</table>

4.4 DATA QUALITY ASSURANCE

The two HemoCue\textsuperscript{®} hemoglobinometers were tested against their respective standard cuvette daily and cleaned regularly. They were calibrated to the correct value whenever the standards showed wrong value.

On days with only the hospital clinic open and no outreach clinics, we examined the same blood sample in both instruments for agreement between them. One instrument showed a slightly higher Hb than the other, on average 5 g/l. This was within the given accuracy limits of the instruments. Adjusting the results of the instrument showing the lowest values, would have given a total mean Hb of 124 g/l instead of 121 g/l.

In order to assess reproducibility of interview-derived variables, some of the interviews were repeated by a different interviewer after a week or more. The variables obtained were compared by kappa analysis, and showed good correspondence. Some selected variables are
shown in Table 7. As expected, the woman’s statement of her own private status was more consistent than her account of her husband’s status.

**Table 7.** Selected kappa values for validation of the antenatal questionnaire, assessed on interviews of 58 of the pregnant women.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Kappa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Woman’s ethnic group</td>
<td>0.8</td>
</tr>
<tr>
<td>Woman’s religion</td>
<td>0.9</td>
</tr>
<tr>
<td>Woman’s age</td>
<td>0.88</td>
</tr>
<tr>
<td>Woman’s literacy</td>
<td>0.9</td>
</tr>
<tr>
<td>Woman’s education</td>
<td>0.95</td>
</tr>
<tr>
<td>Husband’s education</td>
<td>0.84</td>
</tr>
<tr>
<td>Possession of cows</td>
<td>0.75</td>
</tr>
</tbody>
</table>

The mean recall period for verbal autopsies was 6 months, with a range from 3 months to 3 years. We deliberately waited some months, in order to avoid the period of deepest grief. For deaths, recall has been shown to be accurate even after long time.\(^{116,117}\)

A field assistant reviewed all the completed interviews, and then one of the principal investigators reviewed it. The data were entered into an EpiInfo 6.04 database. A second data entry was done for validation of the data, and where errors were detected, they were corrected. The error rate was below 1%, except for spelling errors for alphanumeric variables. The data were converted from EpiInfo to SPSS, and "cleaned" by reviewing frequency tables and checking outliers.

**4.5 ANALYSIS**

The data were analysed using the SPSS versions 7 and 9.

In the cohort study on the outcome of pregnancy, we also used multiple logistic regression analysis to study risk factors for perinatal death, adjusting for parity and prior loss of child, which were potential confounders. In the case series with stillbirths and neonatal deaths, we used chi-square tests and chi-square test for trend to calculate the p-value of the results. The significance level was 5% and all tests were two-tailed.

In the cross sectional study on anaemia, we used multiple linear regression analysis to study the determinants of Hb, and used the regression coefficients (with 95% CI) as a measure of association between Hb and the determinants. In the nested case control study on anaemia, we
used multiple logistic regression analysis to study the determinants (risk factors) of anaemia. The resulting odds ratio was used as an approximation for relative risk. Adjustments were done according to considerations of potential confounders. Generally, we found a need for adjustment for gestational age, altitude, and season.

Because of the high altitude, the distribution of Hb was slightly shifted to the right in our study. In order to compare with studies done at other altitudes, we calculated the corresponding hypothetical Hb at sea level, and applied the anaemia cut-off on these standardised Hb values. The correction factors given by Centers for Disease Control and Prevention (CDC)\textsuperscript{118} was given by broad altitude bands, and no formula for the correction factor was given, though it fits well with a function involving the squared altitude. Based on Hb among children at various altitudes in the Andes, Dirren calculated the association between Hb and altitude by a "Goodness of fit" analysis\textsuperscript{119}:

$$Hb = 3.44 \times e^{(0.00063 \times \text{altitude})} + 116.9.$$  

Based on this equation (with Hb given in g/l), we calculated the following correction factor, to be subtracted from the measured Hb:

$$\text{Hb correction factor for altitude} = 3.44 \times (e^{(0.00063 \times \text{altitude})} - 1).$$  

This closely resembles a simple square function (Fig.7).

**Figure 7.** Altitude correction factor for Hb (g/l) to be added to the measured Hb.

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### 4.6 ETHICAL CONSIDERATIONS

The research protocol was approved by the Regional Committee for Medical Research Ethics in Bergen, Norway, and by the Commission for Science and Technology in Tanzania.
(COSTECH). The permission letter from COSTECH was brought to the Regional Development Director, who issued letters of recommendation to bring forward to the two districts involved. At district level, we introduced the letters to the District commissioners of Hanang and Mbulu districts, who issued new recommendations to bring to the division, ward and village leaders in the study area. With these letters, we introduced ourselves and our objectives and plans to the village leaders, and also requested vital statistics reporting from them. They arranged plenary meetings with the people involved in the household surveys, where we introduced ourselves and presented the objectives and plans for the research. We also had meetings with the administrative staff at the Haydom Lutheran Hospital, and in particular the staff at the MCH clinics.

The participants were also asked individually for oral consent, and those who were found to have anaemia, genito-urinary tract infection, or malaria were offered free treatment. The few women who refused to participate were given the same antenatal service as those who participated. No remuneration was given to the participants.
5 Synopsis of papers

5.1 Paper I: Perinatal mortality in rural Tanzania.
The objective of this paper was to study the perinatal mortality rate and risk factors related to nutrition and infections in a rural population in northern Tanzania. We registered 3618 women attending antenatal clinics and followed them up after delivery. We recorded name, address, date, age, ethnic and religious affiliation, and obstetric history. Further, results of urine nitrite test, Hb concentration, and malaria blood slide result were registered. In a sub sample (also used in Paper IV) we recorded VDRL test and arm circumference. Women who had experienced stillbirths and neonatal deaths were identified and interviewed. No information on the outcome of pregnancy was obtained on seven women and on 99 we had incomplete information.

The perinatal mortality rate was 27/1000 births (95% CI 22/1000 to 33/1000), 44% were early neonatal deaths and 56% were stillborn. There was an increased risk of perinatal death among babies with low birth weight (OR 5.8 for babies 2000-2499 g), among babies of women with a small arm circumference (OR 5.7), among babies of women with positive VDRL serology (OR 5.1), among babies of mothers who had previously lost a baby (OR 1.9), and among babies nulliparous women (OR 1.7).

The perinatal mortality rate was lower than in other studies from Tanzania and East Africa. This was possibly due to a good, accessible and widely used obstetric and perinatal care, and an existing ambulance service which could be requested via a radio-communication system, minimising the delay. Perinatal health improvement may be achieved at antenatal clinics through detection of maternal infections and maternal poor nutrition. Improving survival of babies with low birth weight can probably only be achieved at a hospital with good neonatal care.

5.2 Paper II: Avoidable stillbirths and neonatal deaths in rural Tanzania.
The objective of this paper was to determine the underlying causes of stillbirths and neonatal deaths in the community, and to evaluate whether the deaths were avoidable under the prevailing circumstances. We audited 139 deaths identified through two sources. We identified 119 stillbirths and neonatal deaths in a prospective cohort of antenatal attendees
(described in Paper I) and we identified 21 additional stillbirths and neonatal deaths retrospectively in a household survey in 7 rural communities. One case was reported from both sources. Verbal autopsy was done to reach a diagnosis, in many cases supplemented with information from antenatal records and hospital records. The avoidability of death was assessed for each case, reviewed in light of the existing circumstances. An account of risk factors detectable at antenatal clinic was done by reviewing the ANC cards and ANC registers, and was compared with the woman’s recall of the risk assessment and recall of being referred. Three of the cases were identified but had moved so no verbal autopsy could be done. We analysed 136 cases.

There were 60 stillbirths, 29 early neonatal deaths and 27 late neonatal deaths. Infection-related deaths were most common (n=53, 38%), followed by asphyxia-related deaths (n=32, 23%) and immaturity-related deaths (n=20, 14%). Malaria was the most common infectious agent observed (21 children and 20 mothers). Half of the babies (n=65) were born at home, and slightly fewer died at home (n=55). 21 deaths (15%) were probably avoidable, and 13 (10%) were possibly avoidable. A patient-oriented avoidable factor was identified in 17 cases (51%) and a provider oriented avoidable factor was identified in 22 cases (65%). A maternal risk factor identified at ANC before delivery was present in 26 of the 34 cases of avoidable death, but only two of the women were aware of it, and only one recalled being referred to a hospital for the risk factor.

In this study, the causes of death were similar to other studies in Africa. The relatively low proportion of avoidable stillbirths and neonatal deaths may be partly due to an accessible emergency obstetric care in the area, also reflected in the relatively low perinatal mortality rate. Future efforts should emphasise improving the communication at the antenatal clinics, preparing the women and their families for the delivery, and preparing them for sudden complications.

5.3 Paper III: Anaemia in pregnancy in the highlands of Tanzania.
This study describes the prevalence and determinants of anaemia among rural pregnant women living at 1300-2200 meters above sea level in Northern Tanzania. Between January 1995 and March 1996, 3836 pregnant women from two divisions of Mbulu and Hanang districts attending antenatal clinic were assessed cross-sectionally. Blood samples were examined for hemoglobin concentration (Hb) and thick blood slide (BS) for malaria.
Information on date of examination, village, age, ethnic and religious affiliation, gestational age, and parity was recorded. Altitude was derived from official maps. Main outcome measures were mean Hb and risk of anaemia, defined as Hb less than 9.0 g/dl. The associations between Hb and the determinants were examined in multiple linear regression analysis, and the risk of anaemia (adjusted odds ratio, AOR) was estimated by multiple logistic regression analysis. Adjustments were made for gestational age, season, maternal age and parity.

Mean Hb was 12.1 g/dl, ranging from 4.5 to 18.1 g/dl. Twenty-three per cent had Hb of less than 11 g/dl, 4.6% less than 9 g/dl and 0.5% less than 7 g/dl; standardised to sea level 36.1%, 8.8%, and 1.1%, respectively. The mean Hb increased by 0.3 g/dl per 200 m increased altitude, and the risk of anaemia decreased with a factor of 0.6 per 200 m increased altitude. We found higher risk of anaemia (Hb < 90 g/l) at higher maternal age (1.2 times increased risk per 5 years). Furthermore, the Datoga had twice the risk of anaemia compared with the Iraqw. When going through a pregnancy, the risk of anaemia doubled from 3-4 months of gestation to 7-8 months. The risk of anaemia increased six-fold in the rainy season of 1995, and the risk was almost double among those with malaria parasitaemia.

The findings indicate that anaemia in pregnancy was common in this area of high altitude in rural Tanzania, but less prevalent than indicated by studies from most other parts of the country. The study confirms that preventing anaemia is a challenge in preventive antenatal care in the highlands of Tanzania.


In this paper, we studied the association between anaemia in pregnancy and characteristics related to nutrition and infections. We selected four of the 12 clinics in Paper III (and Paper I) for this study, including the largest at Haydom Lutheran Hospital. We screened 2547 women for hemoglobin (Hb) and malaria plasmodia in capillary blood, and for infections in urine. According to their Hb, they were assigned to one of five groups and selected accordingly, Hb < 70 g/l (n=10), Hb 70-89 g/l (n=61), Hb 90-109 g/l (n=86), Hb 110-149 g/l (n=105), and Hb ≥ 150 g/l (n=50). We aimed at a fairly balanced number in each group, except in the lowest and the highest group where we intended to include all. The difference in
numbers arose because of simultaneous data collection at some clinics. The 312 selected subjects had venous blood drawn and were interviewed, and their arm circumference was measured. The sera were analysed for ferritin, iron, total iron binding capacity (TIBC), cobalamin, folate, vitamin A, C-reactive protein (CRP), and lactate dehydrogenase (LD). Transferrin saturation (Tfsat) was calculated. Urine was examined by dipsticks for nitrite. The associations between anaemia and the determinants were estimated by multiple logistic regression analysis, using adjusted odds ratio as an approximation for risk.

Anaemia (Hb < 90 g/l) was associated with iron deficiency (low s-ferritin: AOR 3.4). The association with vitamin deficiencies were significant in unadjusted analysis (low s-folate: OR 3.1, low s-vitamin A: OR 2.6). Anaemia was also associated with markers of infections (elevated s-CRP: AOR 3.5, urine nitrite positive: AOR 2.4) and hemolysis (elevated s-LD: AOR 10.1). A malaria positive blood slide was associated with anaemia in unadjusted analysis (OR 2.7). An arm circumference less than 25 cm was associated with anaemia (AOR 4.0). The associations with less severe anaemia (Hb 90-109 g/l) were similar but weaker.

The management of anaemia at antenatal clinics should aim at identifying potential infections, particularly malaria, and treating accordingly. Anaemic women without infections should not only be considered for iron deficiency, but folic acid and vitamin A as well.
6 Discussion

6.1 METHODOLOGICAL CONSIDERATIONS

6.1.1 Selection of subjects and potential selection bias

The subjects in our cohort were enrolled through the existing ANC clinics run by HLH. The number of subjects registered in the cohort was 3618 during the 410 days of enrolment. The expected number of pregnancies in the study area during 410 days was 7700 (population 143,000 and local crude birth rate (CBR) 47.7/1000, Paper I), so the study covered approximately 47% of the expected pregnancies in the study area during the data collection. In the household study we found that 90% of pregnant women had been attending an ANC clinic at least once (Paper I).

The study included pregnant women attending 12 ANC clinics run by HLH. In addition, there were 16 other clinics in the area. Since the clinics in the study were run by HLH and therefore belonged to the Lutheran Diocese, one could argue there was a potential selection of women with this denomination. However, women who were not “Protestants” (Catholics or traditional beliefs) were as numerous as the “Protestants” (see Paper I, Table). Usually, the pregnant women would attend the nearest clinic. The belief of the study subject was not a risk factor for perinatal death. We think the selection of study subjects should be fairly representative for the population in the villages covered by the 12 clinics.

No women refused to participate in the cohort study, but some women may have missed registration by avoiding the queue for blood- and urine-test where the recording of the participants took place. A few women had to go home immediately, and could not take time for an interview for the anaemia study.

Some of the study participants (21 of 139) for the study on avoidable still births and neonatal deaths were selected from the household study (Paper II). The household survey covered almost all the households (over 98%) in 7 out of the 42 sub-villages in the area and should give a representative figure. The selection of the sub-villages was done after discussions with the ward leaders, partly based on expected ethnic distribution, partly based on practical and logistical reasons. Potential pregnant women not attending an ANC clinic should therefore be
picked up by this procedure. The cases were however not different from the cases from the cohort.

We observed a generally very positive attitude to the ANC, and we observed an increase in number of attending women during our fieldwork. A woman would often avoid the clinics during the first months of her pregnancy. During the household study, we found some women who had not attended ANC at all during their pregnancy (approximately 10%). Often these were multiparous women who were too busy at home to go to the clinic, and thus did not constitute a large group of “high-risk” women.

Because of the special seclusion practices among the Iraqw and the Datoga which has quite a stigma attached to it, there were probably fewer unmarried women in our cohort than in the general population. Also, ANC being regarded as a modern health care service, it is easily accepted by women with education. In our sample the young and the uneducated may therefore be somewhat underrepresented compared to the population at large. This may theoretically give a lower estimate of the PMR.

6.1.2 Considerations on the outcome measures and determinants

6.1.2.1 Perinatal mortality

The pregnant women in the cohort were followed up until at least one month after delivery. No telephone lines existed for contacting the participants, and most people had no mailing address. Therefore, if a woman did not return to the clinic with her baby, we traced her physically to her home village. The women had registered at the clinic with name, father's name, husband's name, the name of the ten-cell leader, and village. The loss of follow-up may be related to the pregnancy outcome. In seven cases (0.2%) the information on the outcome was completely missing. If all of these pregnancies ended with a death, it would only slightly increase the PMR from 27 to 29/1000. In 106 cases (2.9%), the information on outcome was incomplete. They had either moved out of the study area (51), or their names were unknown by the neighbours and village leaders indicated on their registration (48). It was quite common for people to move, although the majority of the population was fairly stable. One of the reasons for moving might be an ominous incidence such as a death. If the family had moved, we always asked the village leaders and the neighbours for news about the mother and
the baby. Although they could not always confirm survival, they would usually know about a
death, especially if this was the reason for moving.

Follow-up in a developing country may pose serious challenges to achieve acceptable drop-
out rates. A follow up study of outcome of pregnancy in Mozambique resulted in a drop-out rate of 9% of 908 women\textsuperscript{120}, and a study in Malawi had a drop out rate of 2.2 % of 795 women \textsuperscript{121}. Our drop-out (2.9%) rate was comparable with the latter.

We discussed the unknown cases with village leaders and villagers, and reached the
conclusion that they must have registered with a pseudonym and wrong address. Divorce and
remarriage was not rare in this area \textsuperscript{122}, and it was not uncommon that a woman would run
away from her husband, e.g. because of domestic violence. She would then adopt a new
identity and live on with another family, and she would ensure that her former husband could
not trace her. When she got pregnant again, she would usually not inform the staff at the
MCH clinics about this, since revealing her real name posed a risk of being recognised by
people who knew her former husband. We actually managed to identify one woman who had
used a pseudonym and was hiding from her violent previous husband, but generally the
verification of the outcome of pregnancy was impossible in these cases. The PMR among
these women would presumably be (similar or) somewhat higher than the rest of the cohort
because of potentially less favourable health seeking behaviour. If the PMR was doubled
(PMR 60/1000) among the 48 cases with pseudonyms, we might have missed up to three
deaths. This would not seriously influence the mortality estimates of the total population.

There may have been cultural reasons for avoiding exposure for families who lost a baby. As
mentioned earlier, the deaths we were trying to trace were regarded as potentially harmful,
particularly for vulnerable people like newborns and mothers. Usually the women were happy
to share their experience with the interviewer, a doctor whom they had seen during ANC
visits.

Sometimes the follow-up was more cumbersome than we had expected, because the women
often used their Christian or Muslim names when registering at the clinics, whereas they were
known by their traditional names at home. Furthermore, a woman was often known by the
name of her husband, or by the name of her firstborn child, and not by her real name. Another
complication occurred when the father of an attending woman converted to Christianity. The
woman would then register with the father's new name as her family name, and the new Christian name would often be unknown in the village. However, we usually found out by contacting several villagers in the area where we expected to find her.

We do not know whether the women with potentially higher risk (unmarried women, women with a difficult situation at home) were refused attending ANC by their fathers or husbands. As mentioned earlier, the pregnant unmarried women were in meeta and they were therefore regarded as dangerous for other pregnant women. They would avoid crowds and pregnant women, like antenatal clinics. This could introduce a selection bias where unmarried young women and women with a difficult situation at home were underrepresented in the cohort. These women have a potentially slightly higher risk than most women, and therefore our estimate of PMR may be slightly lower than in the general population in the area.

Stillbirths before seven months of gestation were not defined as perinatal deaths. The mother usually knew the approximate gestational age well, even though she often could not indicate the exact dates for the last menstrual period. This inaccurate estimation of gestation poses a risk of misclassification of six-months-stillborn and seven-months-stillborn. We think these will cancel each other out, and the importance is probably minor as they will be of fairly similar age.

Many women (43%) paid their first visit to the antenatal clinic in the last trimester, but less than 10% waited till the last month of pregnancy. In the population of pregnant women, there may have been some women who had a stillbirth before ever attending the clinic. Since the still birth may have precluded the woman from selection into the study by waiting to attend the ANC till late in the pregnancy, it entails a potential bias of underestimating the PMR in the study area. Theoretically, if all women were enrolled at conception, we would find a slightly higher stillbirth rate than we actually found in our cohort. However, in our study there was no difference in the stillbirth rate among women who registered their pregnancy at the ANC early (before 7 months, 15/1000) and later (≥7 months, 15/1000).

6.1.2.2 Causes of stillbirths and neonatal deaths
We used the "Verbal Autopsy" as a tool for assigning a diagnosis as the cause of death. The Standard Verbal Autopsy questionnaire published by WHO\textsuperscript{123} was not available at the time of the study, but we used a questionnaire modified after Smith & Morrow\textsuperscript{124}. The specificity
and sensitivity of the tool varies with the diagnosis, but generally the results are subject to a relatively high degree of misclassification errors. Diagnoses like malaria and pneumonia have achieved a specificity of 90%, but with sensitivities below 50% \(^{125-127}\). The accuracy of the estimates are usually more dependent on a high specificity than a high sensitivity, and also depends on the prevalence of the diagnosis in the material\(^ {128}\). We improved the specificity of the verbal autopsy by using additional information from hospital records. In addition, the interview itself was conducted by medical doctors, increasing the precision of the tentative diagnosis\(^ {129}\). Surprisingly, misclassification in itself does not necessarily decrease the accuracy of the estimate, since over and under-estimation may cancel each other out\(^ {128}\).

Instead of using the specific diagnoses reached by the audit of the verbal autopsies, we classified the diagnoses into functional groups\(^ {130}\), which was partly based on the Wigglesworth classification\(^ {131}\). This grouping improves the performance of the verbal autopsy tool.

The recall of parents is unsatisfactory after minor illnesses, but it is fairly good after serious events such as a death, even after a long time\(^ {116, 127, 132, 133}\). In our study there was good correspondence between information from parents and from hospital, although only a limited number had information from both sources.

**6.1.2.3 Avoidability of stillbirths and neonatal deaths**

The deaths identified through this cohort were studied in detail as a case series ("perinatal audit") to identify the underlying cause of death (diagnosis) and avoidability of the death (Paper II). Some of the information used in this study was based on examinations done during pregnancy. Other information was obtained through an interview with the bereaved family, and gave us information on the symptoms and the circumstances of death.

The case series in paper II was taken from the cohort of attending women as well as from women in the household study. The mortality rates as well as the distribution of causes of death were similar in the two case series. Therefore, we find it unlikely that severe selection bias influences the results based on the cohort.

In paper II we assessed the avoidability of stillbirths and neonatal deaths in an audit. The definition of avoidability that we used was not whether the diagnosis or condition was
theoretically treatable or not, a definition that some authors use. Others evaluate each case individually with assessment of errors or omissions in the management of the condition. We assessed whether the death could or should have been avoided under the prevailing circumstances, thereby indicating possible human errors or omissions, which has been the focus of most of the African studies on avoidable deaths. Therefore, what was unavoidable in this setting could have been avoidable in other settings e.g. treatable under better conditions. This may limit the generalizability of the results to rural areas in developing countries.

During the verbal autopsy interview we also tried to assess the woman's knowledge about her risk factors during the pregnancy that ended in a stillbirth or neonatal death. We asked her: “Did you have any risk factors (Swahili: *vidokezo vya hatari*, literally ‘hints of danger’) on the antenatal clinic card?” Some women responded that they did not know or could not recall. If she answered "no", she would have either no risk factor or would not have been told about any risk factor, or would have misunderstood the message from the midwives. Whichever option, she would have no knowledge of her risk assessment. Her response would therefore indicate her knowledge of the risk assessment, not the absence or presence of risk factors. As described in Paper II, the knowledge of risk assessment was very low among the mothers of the deceased infants, which should encourage midwives to improve their communication. This unsatisfactory result was not surprising. On a busy outreach clinic day, two midwives would serve more than 100 pregnant women. Needless to say, the time spent on each pregnant woman was limited. Furthermore, the women attending the most remote clinics were often not fluent in Swahili, and if the midwife was from another tribe, she would need one of the other midwives or staff to translate for her to obtain any degree of communication. The staff at the clinics were painfully aware of the problem and have later tried to organise themselves in a more rational way.

Through the verbal autopsy we also tried to evaluate whether the deceased woman had been referred to a health facility – higher level of care - during the pregnancy. The pregnant woman would likely not miss this message, though the problem of recall still remains. Our study indicated that the referral system did not function according to the intentions.

As a result, almost no elective caesarean sections were done at Haydom Lutheran Hospital. This is a general problem in Tanzania and other developing countries, and is a
contributing factor to the failure of the risk approach (section 1.2). We think the weakness is probably partly inherent in the system, partly in the mentality of the users of the system. There is a general reluctance to prepare for disaster or complications, in fear of provoking it to happen. A fatalistic attitude, acknowledging God's will in what happen, may make it easier to deal with pain and sorrow after a death, but may undermine the motivation to prepare for the unexpected.

6.1.2.4 Hemoglobin and anaemia in pregnancy

The study design of the Paper III dealing with anaemia was cross-sectional. The study population consisted of the pregnant women in the area. For more than a year (410 days) we selected all the women attending the 12 antenatal clinics run by HLH in the study area for a cross-sectional survey. Some women who were registered had only the urine examination done, and avoided the Hb examination (Fig.6, 14%). Our impression was that some of them were afraid of the finger puncture, and maybe some avoided queuing to save time.

The definition of anaemia has been much debated. WHO criteria for pregnant women define anaemia as Hb below 110 g/l, and severe anaemia as Hb under 70 g/l. The Hb in normal non-deficient pregnant women has a basically normal distribution with mean 112-113 g/l (in the study area). The Hb distribution of anaemic women is wider and with a longer left tail, and it overlaps with the Hb of non-deficient women. Using a fixed cut-off to define anaemia will invariably result in some healthy women with a low normal Hb being defined as anaemic, and some women who usually have a high Hb but now have a reduced Hb (but still above the limit), will be defined as non-anaemic. Hb of 110 g/l may be normal in one woman and too low in another. However, Hb below 90 g/l is always abnormal. Comparing Hb < 90 g/l with Hb ≥ 110 g/l minimised the overlap of the anaemic and the non-anaemic. In our sample, the women with Hb < 70 g/l were too few for sensible separate analysis, and instead we created a group of women with Hb below 90 g/l (by joining the two groups with Hb < 70g/l and Hb 70-89g/l).

In a normal pregnancy, the physiological expansion of the plasma volume leads to a decreasing Hb in the first and second trimesters. The Hb increases a little in the last trimester, giving the characteristic U-shaped curve throughout pregnancy. Several authors and The National Academy of Sciences (USA) have advocated defining anaemia according to the gestational age, e.g. Hb < 110 g/l in first and last trimester and Hb < 105 g/l during second
trimester\textsuperscript{149}. Our participants were measured at different stages of pregnancy, and even though we could not follow each participant regularly \textit{throughout the pregnancy} with Hb, the mean Hb of different women at the various stages reflected the physiologic hemodilution (Fig. 2, Paper III). Applying the arguments above on our study, the women in the second trimester with Hb of 105-110g/l were misclassified as (moderately) anaemic. We have tried to avoid the ambiguity by referring the Hb value and not “anaemia”. The association between Hb and gestational age represented a strong potential confounder for other associations, and we therefore adjusted for gestational age (month) in all the analyses.

The \textbf{instruments} used for Hb measurements were two portable HemoCue\textsuperscript{®} B-Hemoglobin photometers with rechargeable batteries. They were easy to operate and have been recommended as research tools\textsuperscript{150}, but they are somewhat expensive for routine screening procedures in developing countries. The manufacturer indicates an accuracy of 1.5% (corresponding to 2.2 g/l for a “normal” Hb)\textsuperscript{151}. The instrument correlates well with other instruments for Hb measurement, like the Coulter\textsuperscript{150}, but it may read consistently lower, in the order of 3%\textsuperscript{152}. If our instruments read 3% lower than the “true” Hb, the overall actual mean Hb would have been 125 g/l instead of our result 121 g/l, and the prevalence of anaemia with Hb below 110 g/l would be 30.0 % instead of our estimation 36.1 % (Paper III). The test would have better specificity for anaemia, but less sensitivity. Such a systematic error could influence the associations we found and the statistical power of the associations.

Venipuncture of all the women in the cohort was not feasible. Therefore, we used \textbf{capillary} blood to measure the Hb for screening purposes. Capillary blood shows more variation than venous blood\textsuperscript{153,154}. Using the first drop of blood after the puncture does not give acceptable precision\textsuperscript{154}, but drying the first drop and using the next improves the precision. In order to standardise the conditions, we trained the field assistants to a correct sampling technique and supervised throughout the project.

The participants in the study were living at various \textbf{altitudes}, ranging from 1300 to 2200 meters above sea level. We applied Hb standardised to sea-level on the WHO cut-off points of anaemia in order to compare the prevalence of anaemia with other studies. Even though the mean Hb was only slightly reduced by this standardization to seas level (from 121 to 114 g/l), the proportion of women with Hb < 110 g/l increased from 23% to 36% (Paper III). In all the
other analyses of determinants of Hb and anaemia (Papers I-III), we used the measured (not
the “sea-level standardised”) Hb, but adjusted for altitude in the regression models because it
represented a potential confounder in relation to other associations.

Dehydration may influence the Hb by hemoconcentration, resulting in a spuriously high Hb.
The hydration status of the women attending the antenatal clinics was probably not uniform
since there was a marked difference in walking distance between attendees, and hence the
presumed pre-test perspiration and hydration status. We do not have data on the hydration
status on the women, but we would expect a systematically higher Hb among women from
villages distant from the clinic. Analyses of attendants at the HLH clinic showed that women
from distant villages on average had 3 g/l higher Hb than women living close to the HLH (t-
test, p=0.009; regression analysis 2.7 g/l, p=0.015). Dehydration may have masked anaemia in
some of the women with a long walking distance. Supplementary analyses with adjustment
for living place and stratification by clinic showed little effect on the associations studied in
paper I-III. These analyses are not shown in the papers.

6.1.3 Considerations on some of the laboratory examinations
In the analyses of the associations between micronutrients and anaemia (Hb < 90), we found
several significant associations. However, the R² was below 0.3 in all crude (unadjusted)
analyses, meaning that the association explained less than 30% of the variation in Hb. The
highest R² for single determinants was obtained for s-ferritin, which could explain almost a
quarter of the variation in Hb (R²=0.24). Even the full regression model with all the variables
included could explain only 60 % of the variation in Hb (R² just below 0.6). This underscores
the complicated relationship between Hb and the determinants, and warns us to be cautious
about inferences on causality.

Thick blood slides for malaria parasite examination were prepared from capillary blood
taken on the spot on the antenatal visit. The slides were prepared with Field stain and reported
according to the local standard custom, number of parasites per 100 white blood cells (WBC).
This is a semi-quantitative measure, and will be sensitive to changes in the total number of
WBC, e.g. during a bacterial infection. The parasite count (parasites per µL of blood) can
be calculated in samples where the WBC count is available, using the following formula:

Parasite count = [(WBC count) x (Parasites per 100 WBC)/100] per µL
The WBC count was not available to us. There were probably few false positive readings and hence a high specificity, but there may have been a considerable number of false negative slides, since it depends on the number of fields examined, and only a limited number (20) of fields were examined. Such a misclassification may lead to some underestimation of the association with anaemia.

One out of five women had a positive malaria blood slide. However, a positive blood slide does not always imply symptomatic malaria, and a negative slide does not rule out malaria disease\textsuperscript{64,155-157}. The interpretation of the blood slide results may be difficult in a population of partially immune subjects, and its predictive value for malaria disease may be rather low\textsuperscript{158,159}. Thus, the inference we can make is only on the association between anaemia and a positive \textit{blood slide} (read under operational conditions), not the actual association between anaemia and \textit{malaria disease}. More sensitive indicators of malaria disease – but less specific – were the markers of hemolysis (s-LD, s-Haptoglobin, s-ferritin) and the markers of acute phase reaction (s-CRP, s-ferritin). The mechanism for this is evident from the malaria life cycle. Malaria plasmodia invade erythrocytes, mature and multiply through various stages which in the end lead to bursting of the erythrocytes and release of new parasites ready to repeat the cycle. A massive release of malaria parasites often gives rise to fever, malaise and detectable hemolysis, sometimes very severe, causing severe anaemia and jaundice, and the synchronous growth cycles may give the classic recurrent febrile attacks. Some of the new tests for malaria have a very high sensitivity and specificity for detecting malaria parasites in the blood, and are useful for tourists, but not for indigenous people. The people living in the area are semi-immune against the parasites, and may well have parasitized erythrocytes without any symptoms of disease. A continuous exposure to parasites in the blood is actually necessary to keep up the immunity against malaria. Most of the 20\% of pregnant women who had a positive blood slide had no symptoms. Still, the asymptomatic malaria may have a chronic effect on the subjects, and chloroquine prophylaxis has been proven to prevent anaemia and to increase the birth weight. Chloroquine prophylaxis was used at ANC during the study. This is now abandoned due to of drug resistance. Giving presumptive treatment with sulphadoxin-pyrimetamin to pregnant women prevents severe anaemia and possibly improves neonatal survival\textsuperscript{75}. This is currently the official policy for pregnant women in Tanzania.
The use of Norwegian normal reference values for biochemical examinations may not always be appropriate for use in African populations, but lacking alternative reference values, we mostly used the normal reference limits indicated by the laboratory we used in Norway. Many of these are internationally recognised reference values\textsuperscript{114}. Where the normal reference values were disputed, we tested several cut-off values to see the effect on the associations. We could not use the distribution among the participants, because of the selection procedure.

For vitamin A status, we used 0.7 µmol/l as lower normal limit for s-vitamin A indicating low or borderline vitamin A status\textsuperscript{160}. However, vitamin A below 0.35 µmol/l is often regarded as definite deficiency, and both gave similar associations with anaemia and with infections in the analyses.

The C-reactive protein (CRP) is an acute-phase protein that increases early during an inflammatory process. It typically increases steeply during bacterial infections, and also increases during malaria attacks\textsuperscript{155,161}. Viral infections usually have less impact on s-CRP, unless severe inflammation occurs. It also increases in acute inflammatory response of non-infectious origin. In high-income countries, the upper reference limit for s-CRP is often 10 or lower\textsuperscript{114,162-164}, but in pregnancy, the upper reference limit may be as high as 20 mg/l\textsuperscript{165,166}. In many low-income countries with high exposure to infections, the reference limits may be even higher. In our study, we could not use the 2.5-97.5 percentiles of our own sample as a normal reference interval, due to the selection procedure. Since CRP was associated with anaemia, oversampling the anaemic women may have introduced a bias in the CRP distribution. However, we found that among the non-anaemic women, the mean s-CRP was 8 mg/l, the 90-centile was 15 mg/l, and the 95-centile 29 mg/l. Because of this uncertainty with normal reference limits, we analysed the association between anaemia and s-CRP with several cut-off points (5, 10, 15, and 20 mg/l), with similar results. The association had the same direction, but was stronger when using the higher cut-off values, because of a higher specificity as marker of infection, and probably also because it indicated more severe infections. In the analyses presented in paper II, we used 10 mg/l as upper limit for normal s-CRP\textsuperscript{114,162}.

Lactate dehydrogenase (LD) is an enzyme present in all cells. The normal reference limits of LD in serum for adults are 200-450 U/l\textsuperscript{114}, corresponding well with the frequency distribution of s-LD among the study participants with Hb ≥ 110g/l. During necrosis or cell
damage (including hemolysis), the intracellular LD leaks out and the s-LD increases. Hemolysis occurs in malaria infections 64, 167, and malaria parasitaemia was common in the study population. The elevated s-LD was associated with a positive malaria blood slide, and was also highly associated with a low haptoglobin, suggesting hemolysis rather than other type of cell damage. The high correlation between s-LD and s-haptoglobin and s-ferritin is consistent with hemolysis in vivo, and not with hemolysis as an artefact from blood taking and handling. We therefore interpreted an elevated s-LD as a sign of hemolysis due to malaria.

**Ferritin** is the storage protein for iron in the cells, and can be synthesised in any cell when iron supply exceeds the demand. Plasma contains small amounts of ferritin (mostly apoferritin), but increases during cell damage and acute phase reactions. The s-ferritin correlates well with the iron stores in the body, except during acute phase reactions. Malaria attacks also increases the ferritin, and could mask an iron depletion 168, 169. Consequently, we used different normal reference values for s-ferritin according to the s-CRP. For women with a normal s-CRP, a s-ferritin of 15 µg/l was regarded as lower limit of normal iron stores, whereas for women with s-CRP 10 and more, we used s-ferritin below 50 µg/l as lower normal reference limit 115, 170. Transferrin receptor has been suggested as a substitute indicator for iron stores 171, but may have limitations in malarious areas 172. S-transferrin receptor needed strict procedures for taking, separating and storing the sera, and was not available to us.

The body weight of pregnant women is subject to wide variations because of the physiological weight gains, and its usefulness as a determinant is therefore limited. However, the **arm circumference** (AC) has been shown to correlate well with pre-pregnancy body weight 173. Some authors have drawn direct inference from a small AC to poor nutritional status 174, but it should not be done without reservations. Many factors can contribute to a slender arm in adults, including type of food, eating habits, constitution, catabolic states, and physical activity, and this may imply a low specificity for arm circumference to identify poor nutrition. Among non-anaemic women, the 10 percentile was 24 cm, 50 percentile (median) was 26 cm, and the 90 percentile was 29 cm. In our analyses, we used both 22.5 cm and 25 cm as cut-off points as suggested by Krasovec et al., but in paper II the results presented were for 25 cm. Very few women had an arm circumference below 22.5 cm, and consequently even though the direction of the associations were similar, the confidence intervals were wide.
There are several laboratory methods for investigating for syphilis in serum. The VDRL test contains antigens produced from bovine cardiolipin, which initially proved to react strongly with syphilis antibodies, but also with many other antibodies. Cross reactions (biological false positive) have been observed in several infections, like malaria, hepatitis, brucellosis, tuberculosis, and typhoid fever, all common in the study area. In addition, rheumatic conditions may give biological false positive s-VDRL. Its advantage is that it indicates active disease, and becomes negative after the successful treatment of syphilis, unlike the specific Treponema pallidum tests. A study among pregnant women in Malawi indicated that more than half of the VDRL seropositives were not syphilitic. Our study area was probably comparable with Malawi as far as biological false positives concerns, although with a much lower HIV prevalence. The high proportion of positive s-VDRL probably indicates a high prevalence of both syphilis and other chronic infections. The high risk of perinatal loss for women with a positive VDRL may therefore be either due to active syphilis or to the other mentioned diseases.

The birth weight was only measured among the babies born at the Haydom Lutheran Hospital. Immediately after the delivery (within 30 minutes), the babies were weighed on an infant’s beam-balance scale to the nearest 10 g. The birth weight was not available for home births, and the analysis of associations between anaemia and birth weight therefore included only hospital deliveries. There may be a selection bias in two opposite directions of women who deliver in the hospital: the women who are ill may be more likely to deliver in hospital, and the women who are well educated and healthy are also more likely to deliver in the hospital. The first group would have a higher than average perinatal mortality rate, the second a lower rate than average. The Hb was similar among the women delivering in hospital and the others. Further, in home births we found similar associations between perinatal mortality and babies estimated small by their mothers as the associations found in hospital deliveries between low birth weight and PMR.

6.1.4 Events during the study period
We intended to enrol women in the study for at least a year, because seasonal variations in malaria incidence were large and could influence our results. During the rainy season of 1995 there was a severe malaria epidemic in the area, causing a rise in malaria deaths in the Haydom Lutheran Hospital. Cerebral malaria also represented the majority of maternal deaths.
in that period. During the first half of 1995, a higher proportion of the women had detectable parasitaemia (27% versus 14%), and we also observed a lower Hb in the period (117 g/l versus 123 g/l, Fig.3, Paper III). This epidemic had a potential of greatly influencing many of our results, e.g. the PMR, associations between anaemia and CRP, ferritin, vitamin A. However, we performed supplementary analyses not presented in the papers, analysing with adjustment for season and adjustment for malaria parasitaemia, which showed little impact on statistical associations.

During 1995 and 1996, the ANC attendance increased compared to 1994 (39% and 22%, respectively). This was partly because the study project provided extra services free of charge that were not given elsewhere in the area. The presence of a doctor in some of the clinics may also have drawn some attention, especially for women with complications and questions. However, the malaria epidemic probably explains part of the increase, reflected in a more marked increase at the HLH clinic where other hospital services were available.

6.1.5 Power and significance level

We studied many potential determinants. The possibility of falsely detecting an association as significant (Type I errors) increases with the number of determinants studied. By choosing a significance level of \( \alpha = 0.05 \), on average one determinant in twenty (5%) will have a statistically significant association just by chance. This must be taken into account when interpreting positive findings in our material with several determinants.

The study described in paper IV had limited power \( (1-\beta) \) to detect weak associations with anaemia. Therefore, some associations may have been missed due to small sample size (Type II error). However, a weaker association could also indicate less clinical importance. Generally, we wanted to detect the strong and potentially important associations. As expected, indications of iron deficiency (low s-ferritin, s-iron, low s-Tfsat) and folic acid (low s-folate) were associated with anaemia, and also markers of infection (elevated s-CRP, elevated s-ferritin, elevated s-LD, and elevated u-nitrite).
6.2 DISCUSSION OF RESULTS

6.2.1 Perinatal and neonatal mortality rates

In the follow up, we found a perinatal mortality rate of 27/1000 births, 56% of the deaths were stillborn. The neonatal mortality rate was 17/1000 live births. There was an increased risk of perinatal death among babies with low birth weight, among babies of women with a small arm circumference, among babies of women with a positive VDRL serology, and among babies of mothers who had previously lost a baby.

The level of perinatal mortality was lower in our study than what has been reported from other East African studies (Table 8). Infant mortality has declined in many developing countries during the last decades, to a lesser degree neonatal mortality.

Two studies from East Africa (Table 8) found a remarkably low PMR: one from Machakos district in Kenya\textsuperscript{175}, the other from Iringa region in Tanzania\textsuperscript{144}.

The study in Machakos, Kenya, found surprisingly low perinatal mortality rate (46/1000), which was approximately half the national rate in Kenya at that time (1975-78). The authors found the rates almost incredible at first, but indicated several beneficial factors in this area that could explain the lower perinatal mortality: The women and children had a relatively good nutrition, breast-feeding was almost universal, malaria was not holo-endemic (though present), and medical facilities were generally available not too far away. What is not mentioned by the authors, is a possible salutary effect of the demographic surveillance system of visiting homes twice monthly. Women considered seriously ill by the field worker were referred to the project medical staff. Thus, the researchers introduced an “artificially” improved medical care, which may have had a positive effect on the outcome of pregnancy.

In Ludewe, Iringa, Tanzania, the perinatal mortality was estimated to 71/1000 in 1971-76 at Lugarawa hospital\textsuperscript{144}. After an intervention involving changes in obstetric policies, the perinatal mortality was 39/1000. The interventions consisted of active use of partogram with more intensive monitoring of foetal heartbeats, oxytocin augmentation, more active use of assisted labour, and a routine perinatal audit. However, this study was hospital based, and registered only deaths that occurred before discharge from the hospital, and some neonatal deaths may have been missed in this way. Women with uncomplicated delivery usually go
home as soon as possible, often after 1-2 days, and if a death occurred within a week at home, some neonatal deaths would be missed. On the other hand, hospital rates usually overestimate the community rates because of referral of risk pregnancies to hospital, and the two biases do oppose each other.

Table 8. Selected studies on perinatal and neonatal mortality in Tanzania and eastern Africa.

<table>
<thead>
<tr>
<th>District, Region</th>
<th>Rural/ Urban</th>
<th>Year</th>
<th>Sample size</th>
<th>Design</th>
<th>PMR 1</th>
<th>NMR 2</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mbulu/Hanang, Arusha</td>
<td>Rural</td>
<td>1995-96</td>
<td>3618</td>
<td>P, Community</td>
<td>27</td>
<td></td>
<td>Paper I-II</td>
</tr>
<tr>
<td>Mbulu/Hanang, Arusha</td>
<td>Rural</td>
<td>1995-96</td>
<td>370</td>
<td>R, Community</td>
<td>38</td>
<td></td>
<td>Paper II</td>
</tr>
<tr>
<td>Ludewe, Iringa</td>
<td>Rural</td>
<td>1971-76</td>
<td>3102</td>
<td>R, Hospital</td>
<td>71</td>
<td></td>
<td>144</td>
</tr>
<tr>
<td>Ludewe, Iringa</td>
<td>Rural</td>
<td>1977-79</td>
<td>1959</td>
<td>R, Hospital</td>
<td>39</td>
<td></td>
<td>144</td>
</tr>
<tr>
<td>Ilula, Iringa</td>
<td>Rural</td>
<td>1983-86</td>
<td>719</td>
<td>P, Community</td>
<td>82</td>
<td></td>
<td>176</td>
</tr>
<tr>
<td>Morogoro, rural</td>
<td>Rural</td>
<td>1987</td>
<td>3565</td>
<td>R, WHO survey</td>
<td>91</td>
<td></td>
<td>177</td>
</tr>
<tr>
<td>Kilimanjaro, rural</td>
<td>Rural</td>
<td>1987</td>
<td>3565</td>
<td>R, WHO survey</td>
<td>58</td>
<td></td>
<td>177</td>
</tr>
<tr>
<td>Kilombero, Morogoro</td>
<td>Rural</td>
<td>1982-88</td>
<td>88</td>
<td>P, Community</td>
<td>125</td>
<td>81</td>
<td>178</td>
</tr>
<tr>
<td>Kwimba, Mwanza</td>
<td>Rural</td>
<td>1989-90</td>
<td>3056</td>
<td>C-S, Hospital</td>
<td>96</td>
<td></td>
<td>179</td>
</tr>
<tr>
<td>Kwimba, Mwanza</td>
<td>Rural</td>
<td>1990</td>
<td>447</td>
<td>P, Community</td>
<td>68</td>
<td></td>
<td>180</td>
</tr>
<tr>
<td>National, Tanzania</td>
<td>Urban</td>
<td>1982-92</td>
<td>9238</td>
<td>R, Survey</td>
<td>52</td>
<td></td>
<td>181</td>
</tr>
<tr>
<td>National, Tanzania</td>
<td>Rural</td>
<td>1986-96</td>
<td>8120</td>
<td>R, Survey</td>
<td>34</td>
<td></td>
<td>182</td>
</tr>
<tr>
<td>Selected studies from other countries in eastern Africa:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Machakos, Kenya</td>
<td>Rural</td>
<td>1975-78</td>
<td>4768</td>
<td>P, Community</td>
<td>46</td>
<td></td>
<td>175</td>
</tr>
<tr>
<td>Mangochi, Malawi</td>
<td>Rural</td>
<td>1987-90</td>
<td>4031</td>
<td>P, Community</td>
<td>75 4</td>
<td></td>
<td>184</td>
</tr>
<tr>
<td>Maputo, Mozambique</td>
<td>U/R</td>
<td>1994-95</td>
<td>908</td>
<td>P, Community</td>
<td>47</td>
<td></td>
<td>185</td>
</tr>
<tr>
<td>Lungwena, Malawi</td>
<td>Rural</td>
<td>1995-96</td>
<td>795</td>
<td>P, Community</td>
<td>65</td>
<td></td>
<td>121</td>
</tr>
</tbody>
</table>

1 R= Retrospective; P= Prospective; C= Community based; H= Hospital based; C-S= Cross sectional. 2 Perinatal mortality rate = perinatal deaths per 1000 births. 3 Neonatal mortality rate = neonatal deaths per 1000 live births. 4 Rates were given separately for twins and singletons, this figure was calculated.

The level of perinatal mortality rate in our study area was unexpectedly low for a poor rural setting. Some possible explanations may be given. As pointed out in Paper I, we think very few deaths were missed because of dropouts. However, there is still a possibility of missing some attendants, see discussion in section 6.1.1.
Traditional medicine was widely used by a large proportion of people, often in conjunction with modern medicine, and the choice of healer depended on the type of disease or condition. Traditional belief was suggested to contribute to reluctance of use of modern medicine in an Ethiopian study \(^{186}\), but in our study area the people usually had good faith in modern medical services and used it extensively, often in conjunction with traditional medicine. We heard about several traditional healers visiting sick people in the hospital wards. Generally, people had more faith in modern medicine in acute diseases, perhaps reflecting the obvious treatment success. Sometimes a traditional healer could cause delay in serious acute conditions, like cerebral malaria, and we recorded several histories of maternal death where the use of traditional medicine had delayed the treatment. The faith in modern medicine was also reflected in the antenatal clinic coverage above 90\%, and this provided a link to the health system. The antenatal services were free, including all vaccines for mother and child, and the nurses were staff of HLH, a hospital with a good reputation.

In Tanzania, the coverage of health services seems fairly good according to government statistics, and essential and emergency obstetric services are widely distributed throughout the country. However, in many areas of Tanzania, people are not satisfied with the services at the health facilities. Quality of services is often low due to a serious lack of resources and equipment, irregular salaries and hence low working morale. The Haydom Lutheran Hospital was fortunate in this sense, with good equipment, stable supplies, regular salaries, and appropriate medical care. In addition, the hospital was involved in many development projects in the villages: building roads and bridges, water projects, agriculture, secondary schools construction, and was running a well reputed nurse and midwife training school. Therefore, the hospital had credibility for assisting the local people.

The ambulance service at the hospital was quite unique in Tanzania. Very few persons in the area had a motor vehicle, and transport to the hospital was often cumbersome. The hospital had two vehicles that were used as ambulance. They were equipped with VHF-radios linked to solar-powered radio stations in the villages. The ambulance was widely used by ordinary people, not just the most affluent. A study on the ambulance services showed that it was utilised by those who needed it most, and largely independent of socio-economic status \(^{109}\). The relatives of a patient never had to pay the transport bill immediately, but it was added to the hospital bill, giving them more time to find the money. The rapid transport to the hospital
of serious complications of pregnancy probably contributed substantially to the reduction of perinatal mortality. Similarly, the maternal mortality ratio of direct maternal deaths in this area has been shown to be lower than in other areas of Tanzania.

Malnutrition was not common in this area, and nutrition of women and children was fairly good. Experience from the hospital showed that cases of kwashiorkor and marasmus usually were from other districts than the study area. Breastfeeding was universal, but often they would start early with additional feeding. The first few days of life, the newborn would be given only water until the meconium had passed, then starting breast milk and cows’ milk.

The study area was not affluent, but hunger was rare. In cases of crop failure, people would borrow from relatives or buy from other areas with better crops. This system of borrowing and lending constituted something like a social welfare system. Within the area, the distribution of health services was fairly equitable. The interviews of participants indicated that the health facilities were used both by the poor and the well-to-do.

The perinatal mortality rate of Haydom Lutheran Hospital was also lower than in many other hospital based studies in Tanzania (Fig.3, section 3.2.4), supporting the view that there is really a lower PMR in the study area. Hospital rates will normally over-estimate the community rates because of selection of complicated cases.

There is, however, a possibility that selection bias might have influenced the results. However, non-attendance is estimated to only around 10%. Therefore, even if the few women who never attend any modern health facility have higher risk than the rest, this would not seriously affect the results. Using retrospective data from our household study (not dependent on clinic attendance), we found a slightly higher perinatal mortality rate, but consistent with the results in Paper I. As explained earlier (section 3.2.2), the families who lose a baby are in a status of meeta or metid, which means they are stigmatized. When tracing them, the neighbours and leaders may have been reluctant to expose the problem. There may also be burial customs that preclude their exposure to “foreigners” like the investigators, making the tracing delicate and difficult.

In summary, we therefore conclude that in spite of the possibility of a slight selection bias in our study, the PMR is comparatively low.
6.2.2 Risk factors for perinatal deaths

The risk factors for perinatal death that we identified were in line with other studies in Africa. Low birth weight is recognised as the strongest predictor of perinatal death\textsuperscript{121,187}. A very small arm circumference below 23 cm carried a five-fold increased risk of perinatal death (Paper I). A small arm circumference may partly be due to poor nutrition of the women, partly due to heavy energy-consuming physical work. It could also be related to low socio-economic status. Adjustment with indicators of socio-economic status (cows, acreage) did not, however, remove the effect of arm circumference.

A positive VDRL showed a strong association with perinatal death. As pointed out earlier, a positive s-VDRL may not always be due to syphilis. Other chronic diseases giving a positive VDRL serology may also increase the perinatal mortality rate, notably malaria. A positive VDRL may indicate that the woman may have a treatable infection.

Women who had previously lost a child were also at increased risk of perinatal loss. It may indicate that the women have some other conditions predisposing for perinatal loss, and the health workers should always investigate further cases with a bad obstetric history, looking for infections and other treatable conditions. Clinical experience from the area taught us that some women got malaria attacks frequently during pregnancy, others almost never. Prompt treatment of malaria attacks during pregnancy may improve perinatal survival\textsuperscript{75}.

The results gave some optimism on behalf of the potential impact of the health system on the perinatal mortality. A holistic approach is important, including community and facility based health care. A credible surgical service is mandatory for the system to function.

6.2.3 Avoidability of stillbirths and neonatal deaths

The causes of death found in our study are consistent with WHO global estimates (Table 9). Infections, asphyxia related conditions and immaturity-related conditions predominate, in contrast to more affluent countries, where unavoidable deaths predominate, like congenital malformations and extreme preterm birth.
Table 9. Main causes of perinatal deaths.

<table>
<thead>
<tr>
<th>Place</th>
<th>Year</th>
<th>Infection related</th>
<th>Immaturity related</th>
<th>Asphyxia related</th>
<th>Congenital</th>
<th>Other/ Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tanzania; this study</td>
<td>1995-96</td>
<td>39%</td>
<td>20%</td>
<td>32%</td>
<td>7%</td>
<td>16%</td>
</tr>
<tr>
<td>Global, WHO</td>
<td>1986-87</td>
<td>32%</td>
<td>24%</td>
<td>29%</td>
<td>10%</td>
<td>5%</td>
</tr>
<tr>
<td>Jamaica</td>
<td>1979-86</td>
<td>*</td>
<td>19%</td>
<td>44%</td>
<td>6%</td>
<td>32%</td>
</tr>
<tr>
<td>Bangladesh, Matlab, SB</td>
<td>1979-86</td>
<td>13%</td>
<td>27%</td>
<td>31%</td>
<td>*</td>
<td>28%</td>
</tr>
<tr>
<td>Bangladesh, Matlab, END</td>
<td>1979-86</td>
<td>10%</td>
<td>54%</td>
<td>26%</td>
<td>2%</td>
<td>7%</td>
</tr>
</tbody>
</table>

* Infections not specified, antepartum foetal death was 29%.

We found that approximately a quarter of the deaths could possibly have been avoided, granted that the correct steps had been taken when the condition arose. Examples of avoidable factors that might have changed the course of events, were failure to refer a woman with a risk factor to a higher level of care, doctor's failure to recognise the condition in time, failure of woman to contact the hospital when the dangers were apparent, failure to seek help because of lack of persons to take care of the home, or relatives refused the woman to go to the hospital.

Many of the deaths should in theory be easily prevented. In practice, increased alertness and a lower threshold for contacting the health services may be difficult to achieve. Certainly, with the wide coverage of the antenatal clinics, the midwives should encourage the women to have a low threshold for contacting the health services, but this may be undermined if they meet unfriendly staff when they show up. The attitude of the staff may therefore be of utmost importance.

6.2.4 Prevalence of anaemia in pregnancy

The prevalence of anaemia was lower and the average Hb was higher than in other studies from Tanzania (Table 10). The mean Hb was 12.5 as measured, and 12.1 when standardised to sea level. The proportion of women with Hb below 110 g/l was 22.7%, and standardised to sea level 36.1%, and this demonstrates how a high altitude can mask anaemia.
Table 10. Studies on the prevalence of anaemia in Tanzania.

<table>
<thead>
<tr>
<th>Location</th>
<th>Altitude (m)*</th>
<th>Sample size</th>
<th>Gestation (weeks)</th>
<th>Mean Hb (g/l)</th>
<th>Hb&lt;110g/l (%)</th>
<th>Hb&lt;100g/l (%)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mbulu/Hanang, rural</td>
<td>13-2100</td>
<td>3836</td>
<td>16-40</td>
<td>121</td>
<td>23%</td>
<td>67%</td>
<td>Paper I</td>
</tr>
<tr>
<td>(present study)</td>
<td></td>
<td></td>
<td></td>
<td>(114**)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dar es Salaam, urban</td>
<td>0</td>
<td>1317</td>
<td>16-40</td>
<td>93</td>
<td>86%</td>
<td>67%</td>
<td>189</td>
</tr>
<tr>
<td>DSM; Mbagala clinic</td>
<td>0</td>
<td>1391</td>
<td>12-40</td>
<td>98</td>
<td>49%,</td>
<td></td>
<td>190</td>
</tr>
<tr>
<td>Kasarobo clinic</td>
<td>0-900</td>
<td>844</td>
<td></td>
<td>104</td>
<td>66%***</td>
<td></td>
<td>191</td>
</tr>
<tr>
<td>DSM, Hai and Morogoro</td>
<td>844</td>
<td>257</td>
<td></td>
<td>100</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Singida, rural</td>
<td>12-1500</td>
<td>512</td>
<td></td>
<td></td>
<td>11%</td>
<td>192</td>
<td></td>
</tr>
<tr>
<td>Iringga, rural</td>
<td>1300</td>
<td>152</td>
<td></td>
<td></td>
<td>10%</td>
<td>193</td>
<td></td>
</tr>
<tr>
<td>Zanzibar, urban</td>
<td>0</td>
<td>351</td>
<td></td>
<td></td>
<td>92</td>
<td>79%</td>
<td>72</td>
</tr>
<tr>
<td>Arusha, urban</td>
<td>1000</td>
<td>161</td>
<td></td>
<td></td>
<td>41%</td>
<td>194</td>
<td></td>
</tr>
<tr>
<td>Mpwapwa, rural</td>
<td>ca.1000</td>
<td>1148</td>
<td></td>
<td></td>
<td>51%</td>
<td>195</td>
<td></td>
</tr>
<tr>
<td>Mpwapwa, rural</td>
<td>ca 1000</td>
<td>724</td>
<td></td>
<td></td>
<td>61%</td>
<td>196</td>
<td></td>
</tr>
<tr>
<td>Moshi, urban</td>
<td>850</td>
<td>1798</td>
<td></td>
<td></td>
<td>75%</td>
<td>197</td>
<td></td>
</tr>
<tr>
<td>Morogoro urban</td>
<td>600</td>
<td>20</td>
<td>28-39</td>
<td>87</td>
<td>95%</td>
<td>198</td>
<td></td>
</tr>
</tbody>
</table>

* Meters above sea level. ** Adjusted to sea level ***cut-off 105 g/l  DSM=Dar es Salaam

The differences in the prevalence of anaemia can be partly explained by the different altitudes. The study area was situated at a higher altitude, leading to a higher Hb because of the lower oxygen pressure. For example, the study in Moshi was done at a lower altitude (850 m), so a lower mean Hb would be expected (mean Hb was 96.9 g/l). Possibly, rural dwellers had better access to a varied nutrition since most of them were farmers. The other major factors affecting the Hb were gestation, malaria and season (Paper I). This is in line with other studies in the area \(^{54,72}\). The climate is cooler than in the lowlands and less suitable for the breeding of mosquitoes, so that malaria was not holo-endemic. As expected, there was a seasonal pattern of anaemia and malaria, both more frequent in the rainy season.

The effect of other factors was smaller. We found increased risk (doubled) of anaemia among the Datoga women compared to the Iraqw women. The Datoga were more frequent in the lowlands, and adjusting for altitude and malaria parasitaemia reduced the association, but did not remove it. The difference may be due to differences in nutritional habits rather than genetic. Traditionally, the Iraqw were farmers or agropastoralists and the Datoga were cattle herders, though this pattern is less apparent nowadays, as the Datoga settle. The farming traditions may be reflected in a more varied diet for the Iraqw, particularly vegetables, which
may influence the Hb. We find support for this explanation in the material of paper IV, where a low s-folate was more common among the Datoga (30% versus 18% among the Iraqw, not shown in the papers). There was probably little difference in the general nutritional status in the two ethnic groups, since the arm circumference was not different. Other studies have also shown ethnic differences in prevalence of anaemia \(^{199}\), and some authors have even advocated ethnic-specific cut-off values for anaemia \(^{200}\).

There was an increased risk of anaemia with increasing parity and with increasing age (Paper III). However, after adjustment, only age was significantly associated with increased risk of anaemia. We did not find support for the theory that repeated childbearing exhausts the iron stores, but increasing age was associated with anaemia. However, the effect of age was small, Hb decreasing only 1 g/l per 5 years of age. The effect of age is actually less than the precision of the instruments, and the association seems clinically irrelevant. Other authors have found conflicting results regarding parity and anaemia, some have found an association \(^{201, 202}\), others have not \(^{199, 203-205}\).

### 6.2.5 Anaemia, infections and micronutrients

In Paper IV, the study participants were selected by their Hb level (dependent variable) into cases of varying degrees of anaemia to be compared with non-anaemic controls. Studying the associations between anaemia and background factors, it could be regarded as a modified **nested case-control** design and was analysed accordingly. The interpretations of the associations must be done with caution, keeping in mind that an observed association need not be a matter of cause and effect.

The selection procedure in paper IV aimed at approximately equal numbers in each stratum of Hb, but we did not manage to fill up the lowest stratum (Hb < 70 g/l) because of few cases. Unequal numbers were obtained in the various strata because the study was going on at several places simultaneously, and synchronization of selection was impossible. The selection resulted in (intentional) over-sampling of the lower Hb strata, and the associations with determinants were analysed like a case-control study (i.e., Hb < 90 versus Hb ≥ 110 g/l) using the odds ratio as a measure of association. Since the micronutrient status was associated with the Hb, we could not use our sample (which was selected based on Hb) to state the
“prevalence” of various micronutrient deficiencies. Instead, we indicated the proportion with low serum values among women with normal Hb, which is probably representative for non-anaemic women in the population.

Anaemia was associated with markers of infection (S-CRP, S-ferritin). A large proportion of this may be caused by malaria, which was very common in the area, and 15-20% of asymptomatic pregnant women had malaria in their blood slide. It may seem a paradox that the association with parasitaemia was not strong, but it is important to remember that a blood slide has low sensitivity and specificity for residents in areas with malaria. Actually, an elevated S-LD and a low S-haptoglobin may be more specific markers of malaria disease, as they detect minor hemolysis. The risk of anaemia among women with a high s-LD was ten-fold (Table 3, Paper IV).

Infections and malaria has great impact on the interpretation of many of the measurements we had done. In severe anaemia, infections seemed to play an even greater role. The indicators of iron status, folate status and vitamin A status may all be influenced by infections and malaria. The association with micronutrients is therefore best studied among the subjects who had no signs of infections.

Deficiencies of iron deficiency, vitamin A and folate were associated with anaemia, whereas we could not find any association with cobalamin deficiency. A recent study in Tanzania on multiple micronutrient supplementation in pregnancy improved the Hb 206. In a recent trial from Nepal, iron and folic acid supplementation reduced low birth weight, but they did not find any additional benefit with multiple micronutrient supplementation 61. In a large study of vitamin A supplementation, a reduction of maternal mortality was detected 207, but no influence was shown on neonatal weight nor infant mortality 208.

Previous interventions to reduce anaemia in pregnancy have included supplementation of iron and folic acid, and malaria prophylaxis. Even though proven efficacious, scarce resources and poor compliance have limited the impact of these simple and inexpensive interventions.
6.3 MAIN CONCLUSIONS AND RECOMMENDATIONS

Based on the findings in this study, we conclude as follows:

1. The perinatal mortality (PMR) in this study was lower than what has been found in other studies from Tanzania. This indicates that the existing health system may give better results when implemented properly, and when emergency obstetric care is quickly available.

2. Determinants associated with perinatal death were low birth weight, mother’s small arm circumference, infections in mother, previous loss of baby, and primiparity. Anaemia, malaria, urinary tract infections in pregnancy were not significantly associated with perinatal death.

3. Main causes of perinatal and neonatal deaths were infection related (39%), asphyxia related (23%), and immaturity related (14%).

4. Even though the PMR was low, a quarter of the deaths could probably have been avoided either by the mother or the family, the midwife or the doctor. Future efforts should emphasise improving the communication at the antenatal clinics, continue preparing the women - and their families - for the delivery and to be ready for complications.

5. The prevalence of anaemia in pregnancy was substantial (36%), but lower than what has been found in other areas of Tanzania. The low prevalence could partly be explained by a high altitude, partly a fairly good nutrition, and partly to less prevalence of intestinal worms than many other areas in Tanzania.

6. Determinants of anaemia were high age, Datoga ethnic group, and rainy season. Furthermore, iron deficiency, folate deficiency, vitamin A deficiency, high CRP, high ferritin, high LD, malaria in blood, and u-nitrite were also related to the prevalence of anaemia, as was also an abnormally lean stature. Management of severe anaemia should ensure that the subject in question is not just given micronutrients, but also is examined for possible malaria or other infections.
7 References

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82. Rekdal OB. The invention by tradition: creativity and change among the Iraqw of northern Tanzania [Dr.polit.thesis]. University of Bergen, 1999.


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105. Bura M. Pregnancy and child rearing practices among the Wa-iraqw of Tanzania [Diploma]. Liverpool School of Tropical Medicine, 1984.


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8 Appendices

The questionnaires for the research were written in Swahili, but are here reproduced in English versions.

Research permit in Tanzania was given for one calendar year, only the first permit is shown here. Also, the clearances at regional level and district level are not shown here.

Questionnaires:
- Questionnaire for antenatal visit
- Questionnaire for visit after delivery
- Questionnaire for verbal autopsy for deceased infants

Research clearances
- Research permit, Tanzania, COSTECH
- Ethical clearance of research, Norway
8.1 QUESTIONNAIRE FOR ANTENATAL VISIT

1. All information is to be kept confidential by interviewer and anyone who is involved in the project.
2. If the respondent refuses to answer the questionnaire, please write this on the front page. If the respondent refuses to answer specific questions, please write an R in the right margin beside the specific question.

ANTENATAL CLINIC SURVEY

To be filled in for women attending antenatal care and who are included in the Urinary Tract Infection and Anaemia studies.

Is willing to answer questionnaire: Yes: ___ No: ___
If not willing, please enter all information up till Q.3
Date of interview: ______________________
Name of interviewer: _________________________________________
Place of interview (MCH clinic): ______________________________
MCH clinic registration number: _______________________

1. Mother’s name: ______________________________ Clan: ______________
2. Mother's tribe: __________________________ Religion: ______________
3. Mother’s address: Ten-cell leader:
   Kitongoji (place): __________ Village: __________
   Ward: ______________
4. Mother's age in completed years: _______ (Tick one of the following).
   _____ Age based on date of year of birth
   _____ Age based on estimate
5. Mother's place of birth: Village: ______________ Ward: __________
6. Does the mother wear a "hanang’wenda" (skin skirt)? Yes: ___ No: ___

7. Husband’s name: __________________________ Clan: ______________
8. Husband's tribe: __________________________ Religion: ______________
9. Husband’s address if different from above:
   Ten-cell leader: __________________________
   Kitongoji(place): ________________________ Village: ______________
   Ward: __________________________
EDUCATION / OCCUPATION

1. Completed years of education:

   Male     Female
   _____     _____  Primary:
   _____     _____  Secondary:
   _____     _____  Training of other types:

   Yes      No     Yes      No
   ___      ___    ___      ___  Can you read?
   ___      ___    ___      ___  Can you write?

2. What types of work is done to earn money for the family? (Several ticks may be made.)

   Male     Female
   Yes      No     Yes      No
   ___      ___    ___      ___  Farmer
   ___      ___    ___      ___  Keeping Livestock
   ___      ___    ___      ___  Brewing beer
   ___      ___    ___      ___  Owner of business: Specify:______________
   ___      ___    ___      ___  Employed in business: Specify:______________
   ___      ___    ___      ___  Employed in other institution; Specify type:____
   ___      ___    ___      ___  Not employed, and looking for employment:
   ___      ___    ___      ___  Student:
   ___      ___    ___      ___  Other ways of getting money, specify:______

3. Does the mother have any income other than the husband's?  Yes___ No___
   If YES, please specify:______________________________

HOUSEHOLD/SANITATION/INCOME/TRANSPORT

1. In the household where you are living how many are there of the following?

   Number
   _____  Cattle
   _____  Goats
   _____  Sheep
   _____  Pigs
   _____  Chicken
   _____  Ducks
   _____  Others; specify ____________
2. How many acres of shamba does the family of this household have? ______

3. What is grown on these acres?

<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>______</td>
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<td>______</td>
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<td>____</td>
</tr>
</tbody>
</table>

4. How many of these acres are grown for household use only? ______

5. How many of these acres are grown for sale? ______

6. Does the household have enough food for their own needs? Yes No

7. If no, what do they do when they need extra food? Specify:___________

8. How many houses does the family have to live in at your dwelling place? __

9. What type of housing is the residence where you sleep?

   a) Walls:
   - Mud/earth
   - Straw
   - Bricks
   - Cement
   - Other; specify:____________________

   b) Roof:
   - Bati
   - Straw
   - Earth
   - Other; specify:____________________

10. Number of rooms in your residence where you sleep: ______

11. Do cows and other livestock stay in your main house where you sleep at night? Yes No

12. Are there ticks in the walls of the house where you sleep? Yes No
13. In the household where you live, what is the main source of water?

SEASONS
Rain  Dry

Piped water:
___ ___ Piped into residence
___ ___ Public tap

Well water:
___ ___ Well in residence/yard/plot
___ ___ Private well outside plot
___ ___ Public well

Surface water:
___ ___ Spring
___ ___ River/stream
___ ___ Pond/lake
___ ___ Dam

Other sources:
___ ___ Rain water
___ ___ Tanker truck
___ ___ Bottled water
___ ___ Other: Specify: _______________________

14. How much time does it take to walk to source of water, fetch water, and come back?

SEASONS
Rain  Dry
___ ___ None (piped in to household)
___ ___ Some, but less than an hour
___ ___ 1 to 2 hours
___ ___ 2 to 3 hours
___ ___ 3 to 4 hours
___ ___ More than 4 hours

15. Who fetches the water? (Several ticks may be made if it varies)
___ No one, not applicable
___ Children
___ Adult women
___ The person being interviewed
___ Adult men
___ Ox cart/donkey
___ Trucks or other vehicles
___ Others   Specify _______________________

89
16. How is refuse disposed of in this household?

____ Pit, buried
____ Pit, open
____ Open field
____ Burned
____ Lake or river
____ Other Specify _____________________________________

17. What type of toilet facilities does the household have?

____ Water flush toilet
____ Pit latrine
____ None
____ Other Specify _____________________

18. What is the distance from the main residence where you live to health care facilities? (The number of hours of walking time for the respondent should be specified to nearest half hour).

<table>
<thead>
<tr>
<th>Name</th>
<th>Hours (Walking)</th>
<th>Which is the nearest antenatal clinic</th>
<th>Which antenatal clinic is actually used</th>
<th>Which is the nearest dispensary/health centre</th>
<th>Dispensary/health centre used most commonly</th>
<th>Which is the nearest hospital</th>
<th>Which hospital is used most commonly</th>
<th>Haydom Hospital</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

19. Is there access to transportation by car or bus from your main residence to the following health facilities?

<table>
<thead>
<tr>
<th>Name</th>
<th>No</th>
<th>Sometimes</th>
<th>Steady</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Nearest antenatal clinic
Antenatal clinic actually used
Nearest health centre/ dispensary
Dispensary/health centre used most
Nearest hospital
Hospital used most commonly
Haydom hospital

20. If there is access to any transport, what type of transport is available to the following facilities?

Hospital: Explain: __________________________
Dispensary/Health Centre: Explain: __________________________
Antenatal Clinic: Explain: __________________________

21. What type of transport is available to Haydom Hospital?

Specify: ________________________________________
MOTHER'S STATUS

(For all these questions, be extra polite and if interviewer thinks it may be necessary, ask more indirectly to get a correct answer.)

1. What is your marital status?
   Yes   No
   ___  ___  Are you presently married
   ___  ___  Are you presently divorced
   ___  ___  Are you presently widowed
   ___  ___  Are you presently single/unmarried
   ___  ___  Other: Specify: ___________________________

2. If you are married, is your husband living in the same household as you?         Yes____ No____
   If NO, who do you get help from? Explain:____________

3. If you are not married, where do you get help from? Explain:______________

4. Have you been married several times?       Yes____ No____
   If YES, how many times have you been married including present marriage? __

5. How old were you the first time you married?________

6. Does your husband have more than one wife?          Yes____  No____
   If YES, how many wives does he have, including you? ______
   Which number of wife are you? _____

MOTHER'S HEALTH STATUS

7. What was your estimated age at menarche?    _____   years

8. What was your age when you had your first pregnancy (time of conception)?        _______    Years
   (Here the interviewer may try to use certain events that are commonly known in order to get correct year)

9. Have you had any vaccinations when you were:
   Yes   No  Don't know
   ___  ___  ___       A Child
   ___  ___  ___       Pregnant

10. Have you ever had any surgical operations?  Yes__ No___ Don't remember___
    If YES, which?
    ___       Abdomen
    ___       Gynaecological
    ___       Bones
    ___       Others; specify:_____________________

11. Have you ever had blood transfusions?       Yes___ No___ Don't know___
12. Have you had any of the following diseases diagnosed at a health facility?

BEFORE (within 6 months before the beginning of this pregnancy); PRESENT (present pregnancy)

<table>
<thead>
<tr>
<th>Before</th>
<th>Present</th>
<th>Don't know</th>
<th>Before</th>
<th>Present</th>
<th>Don't know</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>No</td>
<td>Don't know</td>
<td>Yes</td>
<td>No</td>
<td>Don't know</td>
</tr>
<tr>
<td>______</td>
<td>______</td>
<td>______</td>
<td>______</td>
<td>______</td>
<td>______</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Thromboembolic disease (blood clots)</td>
<td>Heart disease</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>______</td>
<td>______</td>
<td>______</td>
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<td>______</td>
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<tr>
<td>Hypertension (high blood pressure)</td>
<td>Epilepsy</td>
<td>Malaria</td>
<td></td>
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<td>______</td>
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<td>______</td>
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<tr>
<td>Relapsing fever (ticks)</td>
<td>Diarrhoea</td>
<td>Amoeba</td>
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<td>______</td>
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<tr>
<td>Severe urinary tract infection</td>
<td>Gynaecological disease</td>
<td>Kidney disease</td>
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<td>______</td>
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<tr>
<td>Lung disease (pneumonia etc)</td>
<td>Tuberculosis</td>
<td>Liver disease (jaundice)</td>
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</tbody>
</table>
| Severe skin infections | Sexually transmitted disease, (ex. Gonorrhoea, Syphilis, Trichomonas) | Others; specify: _________

13. Has your mother or any of your sisters had any of the following conditions during pregnancy, delivery or shortly after delivery?

<table>
<thead>
<tr>
<th>Condition</th>
<th>Yes</th>
<th>No</th>
<th>Don't know</th>
<th>Mother</th>
<th>Sister</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cramps or convulsions</td>
<td>______</td>
<td>______</td>
<td>______</td>
<td>sister_______ mother____</td>
<td></td>
</tr>
<tr>
<td>High blood pressure</td>
<td>______</td>
<td>______</td>
<td>______</td>
<td>sister_______ mother____</td>
<td></td>
</tr>
<tr>
<td>Swollen body</td>
<td>______</td>
<td>______</td>
<td>______</td>
<td>sister_______ mother____</td>
<td></td>
</tr>
<tr>
<td>Albumin in urine</td>
<td>______</td>
<td>______</td>
<td>______</td>
<td>sister_______ mother____</td>
<td></td>
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</tbody>
</table>

14. What would you have liked the MCH clinic from Haydom hospital to have assisted you with during this pregnancy? Specify: ______________
USE OF STIMULANTS AND MEDICINE

(For these questions as well, be extra sensitive, and if interviewer finds it necessary, please use a more indirect approach)

1. Do you smoke tobacco?   Yes:____ No:____
   If NO, have you smoked in the past?   Yes:____ No:____
   If YES, at what age did you start smoking?   Age:____
2. For how many years have you smoked?   Years:____
3. Have you been smoking the last 30 days?   Yes:____ No:____
   If YES, how many cigarettes do you smoke presently per day?   Number:____
4. If you smoke or sniff or chew any other type of tobacco presently other than cigarettes, please specify the type and amount per day.   Specify:________
5. Did you drink any of the following the last 30 days?
   Yes No
   ____ ____ Soda
   ____ ____ Pombe(local brew)
   ____ ____ Beer
   ____ ____ Milk
   ____ ____ Konyagi
   ____ ____ Piwa (locally distilled alcohol)
6. What amount did you take of each of the following:
   Soda Pombe Beer Milk Konyagi Piwa
   Yesterday: ______ ______ ______ ______ ______ ______
   Total amount last 7 days: ______ ______ ______ ______ ______ ______
7. Do you take any medicines on a regular basis presently?   Yes:____ No:____
8. If YES, please specify the type and amount.   Specify:_______________
9. What kinds of traditional medicine did you use within the last 30 days?   Specify:_______________
10. Are you circumcized?   Yes:____ No:____ Don't know:____
## OBSTETRIC HISTORY
Previous pregnancies, first pregnancy no.1, second preg. no.2 and so on.

<table>
<thead>
<tr>
<th>No. of pregnancy</th>
<th>Year</th>
<th>Outcome</th>
<th>Months of pregnancy</th>
<th>Baby: kg</th>
<th>Sex</th>
<th>Lactating months</th>
<th>Place of delivery</th>
<th>Place of planned delivery</th>
<th>Who helped</th>
<th>Mode of delivery</th>
<th>Complications for mother:</th>
<th>Child of child’s death</th>
<th>Cause of death</th>
<th>Age at death</th>
<th>ANC</th>
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8.2 QUESTIONNAIRE FOR VISIT AFTER DELIVERY

REPRODUCTIVE HEALTH PROJECT

1. All information is to be kept confidential by interviewer and anyone who is involved in the project.
2. If the respondent refuses to answer the questionnaire, please write this on the front page.
   If the respondent refuses to answer specific questions, please write an R in the right margin beside the specific question.

VISIT AFTER DELIVERY

These questions should be answered by mother after delivery, usually after 2-3 months.
Is she willing to answer questionnaire: Yes:____ No:____
If not willing, please enter all information up till question 2.

Date of interview:____________________________
Name of interviewer:________________________________________________
Place of interview (MCH clinic):_______________________________________
MCH. Reg. No.:____________________________________________________

1. Mother's name:_____________________________________________ Clan:___________________
2. Mother's address
   Ten-cell leader:________________________
   Subvillage (Kitongoji):_______________ Village:_____________________
   Ward:__________________________________
3. Is the mother alive?  Yes:____ No:____
   If NO, how many days after delivery did she die? ________
4. Child's name:_________________________________________ Sex:______ M/F
   2nd Twin:_____________________________  Sex:______ M/F
   3rd triplet:___________________________  Sex:______ M/F
5. Date of birth:___________________________________________
6. Age today: Weeks:________ (2nd Twin) Weeks:_______
7. Body weight today: Grams:______ (2nd Twin) Grams:______
PREGNANCY

8. What was the gestational age at this delivery? Weeks:____________

9. How many children were born of this pregnancy?______

10. Did you have any problems in this pregnancy? specify: _________________

11. Did you have problems with any of the following? (Several ticks may be made.)

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12. If you had problems, how did you get help? Explain:__________________________
13. Place of delivery: (specify village): ______________________
   - Home
   - At relative's or friends house
   - Road side
   - In vehicle
   - Health centre/ dispensaries
   - Haydom Hospital
   - Other hospital
   - Other; specify: _______________________________________

Who assisted you: Name: _______________
   - doctor
   - midwife
   - TBA
   - mother-in-law/mother
   - other; specify: _______________________________________

14. Where did you plan to deliver?
   - hospital
   - dispensary
   - home
   - other; specify: _______________________________________

15. If you did not deliver where you planned to, why?
   - Service too expensive
   - Not accepted by family; Why? _________________________
   - Not enough time after birth started
   - Transport not available
   - Other; specify: _______________________________________

16. Child's bodyweight/size/height when born  (2 T. = 2\textsuperscript{nd} twin)

   Bodyweight  Grams: ______  (2 T. Grams: _____)
   Size:  Big: ______  (2 T. Big: ______)
   Medium: ______  (2 T. Medium: _____)
   Small: ______  (2 T. Small: _____)
   Height: cm: ______  (2 T. cm: _____)
17. Was it difficult to get the baby out?

Yes:___  No:___  
(2 T. Yes:___  No:___)

If YES, Why?

___ very big baby  
(2 T. _____)

___ mother's pelvis was narrow  
(2 T. _____)

___ other;  
(2 T. _____)  specify:__________

18. What was the presenting part?

___ Head  
(2 T. _____ head)

___ Breech  
(2 T. ______ breech)

___ Other  
(2 T. ______ other)  specify:__________

19. Did the baby cry within one minute after delivery?

Yes:___  No:___  
(2 T. Yes:___  No:___)

20. What was the umbilical cord cut with?

___ new razor blade

___ used razor blade

___ knife

___ arrow (special for bleeding cows)

___ peeling of sugar cane

___ hospital equipment

___ other; specify:__________________________________

21. After cutting the umbilical cord, what did you put on the cord?

___ thread

___ medicine

___ nothing

___ tendon thread

___ hospital equipment

___ other; specify:__________________________________

22. Was the baby able to suck mothers milk just after birth?

Yes:__  No:__  Didn't get chance:__  
(2 T. Yes:__  No:__  Didn't get chance:__)

If NO, or Didn't get chance, Why?:__________________________
23. In the first week the baby got: (Several ticks possible)

<table>
<thead>
<tr>
<th></th>
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<td>Cow's milk</td>
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<td>other;</td>
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</table>

specify:_____________________

24. Within the first month (30 days), the baby had:

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No</th>
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<tr>
<td>Fever</td>
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If YES; Explain:_________________________

| Diarrhoea         |     |    |

If YES; Explain:_________________________

| Cough             |     |    |

If YES; Explain:_________________________

| Wasted            |     |    |

If YES; Explain:_________________________

| Accident          |     |    |

If YES; Explain:_________________________

25. When your child was ill where, how was he/she helped?

Explain:__________________________________

26. Is the child in good health now? Yes:___ No:___

If NO, explain:________________________________

MOTHER'S PROBLEMS WITH DELIVERY AND 6 WEEKS THEREAFTER

27. Was there bleeding before delivery (APH)?: Yes:___ No:___

If YES, what type of help did you get? Explain:_____________________________

28. Was there excessive bleeding after delivery (PPH)?: Yes:___ No:___

If YES, what type of help did you get? Explain:_____________________________

29. When did the placenta come out?

____ within an hour after the child

____ more than one hour after the child
30. Did you get fever after the delivery?  Yes:___ No:___
   If YES, when did it occur after delivery: Day:_________
   What was the fever like?  Several ticks may be made.
   ____ very high
   ____ average
   ____ low
   ____ intermittent
   ____ continuous
   What did you do to get better? Explain:__________________________

31. Have you had cramps or convulsions?
   ____ no
   ____ yes, before delivery
   ____ yes, during delivery
   ____ yes, after delivery

32. Did you get any problem after delivery?  Yes:___ No:___
   If YES, explain:___________________________________________

33. Have you had problems controlling any of the following due to previous deliveries:
   Stool?       Yes:____ No:____
   Urine?      Yes:____ No:____
   What kind of help did you get? Explain:_______________________

34. Are you in good health now?  Yes:__ No:__
   If NO, specify the problem:_______________________________

35. If you had problems during delivery and up till 6 weeks after delivery, how did you get help?
   Explain:_________________________________________________
FAMILY PLANNING

1. As you may know, there are various ways that a couple can delay the next pregnancy or avoid pregnancy. Do you know of any of these methods?
   
   Yes: ___ if yes, go to 2
   No: ___ if no, go to 3

2. a) Which methods do you know of? ________________________________
   Do you know any others? ________________________________
   
   Yes No
   ___ ___ b) Have you ever used that (those) method(s)?

3. One way a woman can delay the next pregnancy, or avoid getting pregnant, is to take a PILL every day.
   
   Yes No
   ___ ___ a) Have you ever heard of this method?
   ___ ___ b) Have you ever used this method?

4. A woman may have an INJECTION every three months to avoid pregnancy.
   
   Yes No
   ___ ___ a) Have you ever heard of this method?
   ___ ___ b) Have you ever used this method?

5. A woman may have a LOOP or A COIL of PLASTIC or METAL, THE INTRAUTERINE DEVICE, inserted in her womb by a doctor and left there.
   
   Yes No
   ___ ___ a) Have you ever heard of this method?
   ___ ___ b) Have you ever used this method?

6. She may also place a DIAPHRAGM or TAMpon or SPONGE in herself, or use FOAM TABLETS or JELLY or CREAM.

   Yes No
   ___ ___ a) Have you ever heard of these methods?
   ___ ___ b) Have you ever used any of them?
7. Some women wash themselves immediately after sex, with WATER or some other liquid.
   
   Yes  No
   ___  ___ a) Have you ever heard of this method?
   ___  ___ b) Have you ever used this method?

8. There are also some methods men use so that their wives will not get pregnant. Some men wear a CONDOM during sex.
   
   Yes  No
   ___  ___ a) Have you ever heard of this method?
   ___  ___ b) Have you and your husband ever used it?

9. Some couples avoid having sex on particular days of the month when the woman is most able to become pregnant. This is called the SAFE PERIOD or RYTHM METHOD.
   
   Yes  No
   ___  ___ a) Have you ever heard of this method?
   ___  ___ b) Did you and your husband ever do this?

10. Some men practice WITHDRAWAL, that is, they are careful and pull out before climax.
    
    Yes  No
    ___  ___ a) Have you ever heard of this method?
    ___  ___ b) Did you and your husband ever use this method?

11. Another way of avoiding getting pregnant is to GO WITHOUT SEX for several months or longer.
    
    Yes  No
    ___  ___ a) Have you ever heard of this method?
    ___  ___ b) Have you ever done this to avoid getting pregnant?

12. Some women have an operation, called STERILIZATION, having their tubes tied, in order not to have any more children.
    
    Yes  No
    ___  ___ a) Have you ever heard of this method?
    ___  ___ b) Have you had a sterilization?
13. Some men have a sterilization operation, called VASECTOMY, so that wives will not have more children.
   **Yes**  **No**
   ___ ___ a) Have you ever heard of this method?
   ___ ___ b) Has your husband had vasectomy?

14. Have you ever heard of any other method which women or men use to avoid pregnancy?
   Specify: __________________________________________________________
   **Yes**  **No**
   ___ ___ a) Have you and your husband ever used this method?

15. I want to make sure I have the correct information. Have you ever done anything or tried to delay or avoid getting pregnant?
   **Yes**  **No**
   ___ ___ Specify: __________________________________________________

16. Do you wish to have more children?
   **Yes**  **No**
   ___ ___

17. If yes, how many more do you wish to have?
   Total:____  Boys:____  Girls:____  Don't know:____

18. Do you and your husband agree on this matter?
   Yes:____  No:____  Haven't discussed it:____

19. If you don't agree, in what way do you not agree?
   Specify: __________________________________________________________
8.3 QUESTIONNAIRE FOR VERBAL AUTOPSY FOR INFANTS

CONFIDENTIAL

VERBAL AUTOPSY FOR INFANTS

INTERVIEW

1. Interviewer: ________________________________
2. Respondent: _________________________________
3. Respondent's Relation to the child: __________
4. Date of interview: ________________

PERSONALIA

5. Child's names: __________________________________
6. Sex (M/F): __
7. Liveborn (Y/N): ___
8. Ethnic group: __________
9. Religion: __________
10. Mother's names: __________________________ Age: ___ Living (Y/N): ___
11. Father's names: __________________________ Age: ___ Living (Y/N): ___

ADDRESS

12. Ten Cell Leader (Balozi): ______________________
13. Kitongoji: ______________________
14. Kijji: ______________________
15. Kata: ______________________

CHRONOLOGY

16. Date of birth: _________ Exact: ___ Guessed: ___
17. Date of onset of sickness: _________
18. Date of death: _________
19. If mother died, mother's date of death: _________
CIRCUMSTANCES OF DEATH

20. Was the child seen during the last illness by:
   __ village health worker?
   __ trained nurse?
   __ doctor?
   __ traditional healer?
   __ other, specify: ________________________

21. Was the child admitted to hospital during the final illness? Y/N___

22. Where did death occur?
   __ home
   __ dispensary/health centre
   __ hospital
   __ other, specify: ________________________

RESPONDENT’S ACCOUNT OF DEATH

23. What does the respondent consider as cause of death, and how did it occur?
   ______________________________________________________________________
   ______________________________________________________________________

OBSTETRIC HISTORY

24. Fill in obstetric history for child’s mother on the last page.
25. How many other deliveries has she had before? ___
26. How many children to the mother are now alive? ___
27. What is the age of the last child (months)? ___
28. How many tetanus toxoid did she receive this pregnancy? ___
29. How many TT did she receive in other pregnancies? ___

INDEX PREGNANCY

30. Did the mother attend ANC this pregnancy? Y/N__
   If YES, -do you have the card? Y/N
       -where did she attend? ____________________
       -how many times? ___
       -did she attend for problem or routine? P/R ___
       -did she receive any treatment? Y/N ___
       -did she have risk factors noted on the card? Y/N ___
       -was she referred? Y/N ___
           If YES, to where/who: ____________________
31. Did she have any problems in this pregnancy? Y/N:__
   Please specify: _______________________________________________________
   Did she have problems with any of the following during pregnancy?
      Yes      No
   ___      Don't know
   ___      Swelling of the body
   ___      Excessive tiredness
   ___      Malaria
   ___      Operation: (specify type)_____________________
   ___      Fever
   ___      Excessive vomiting
   ___      Diarrhoea
   ___      Amoeba
   ___      Weight loss
   ___      Dizziness:
   ___      Anaemia:
   ___      Infections (specify):
   ___      Other diseases (specify):
   ___      Too heavy work load
   ___      Not enough food
   ___      Depression
   ___      Social problems: (specify)
   ___      Husband drinks excessive amount of pombe (local beer)
   ___      Husband sells crops/livestock to get pombe
   ___      Other problems (specify):

32. How did she get help?(where, what kind of help, did she get better)
   Explain:_________________________________________________________________________________

33. Was the baby delivered before death?__

34. What was the gestational age? Weeks:______ Don't know:____

35. How many children were born of this pregnancy? ___ Don't know:___
   If TWINS,
   - name of other twin:___________________
   - is other twin alive? Y/N:__
   - who came first?___________________
36. Place of delivery: (specify village): __________________________
   ____ Home
   ____ At relative's or friends house
   ____ On the road side: Explain:
   ____ In vehicle: Explain:
   ____ In ambulance: Explain:
   ____ Health centre/dispensary
   ____ Haydom Hospital
   ____ Other hospital
   ____ Other; specify: _______________________________________
   ____ Don't know

37. Who assisted the delivery: Name: ____________________________
   ____ doctor
   ____ midwife
   ____ TBA
   ____ mother-in-law/mother
   ____ other; specify: _______________________________________
   ____ don't know

38. Where did she plan to deliver?
   ____ hospital
   ____ dispensary
   ____ home
   ____ other; specify: _______________________________________

IF she did not deliver where she planned to, why?
   ____ Service too expensive
   ____ Not accepted by family; Why? ___________________________
   ____ Not enough time after birth started
   ____ Transport not available
   ____ Other; specify: _______________________________________

39. For how long was she in labour? __ hrs

40. Mode of delivery:
   ____ Normal
   ____ Vacuum
   ____ Forceps
   ____ Breech
   ____ Cesarian Section
   ____ Other: _______________
41. Was it difficult to get the baby out?
   No: ___ (twin No: ___)
   Yes: ___ (twin Yes: ___)
   If YES, why? ___ very big baby
   __ mother's pelvis was narrow
   ___ other; specify: ______________________

42. What was the presenting part?
   ___ Head (twin: ___ head)
   ___ Breech (twin: ___ breech)
   ___ Other (twin: ___ other), specify:_____________

43. What was the cord cut with?
   ___ new razor blade
   ___ used razor blade
   ___ knife
   ___ arrow (tsaxara/shawuda)
   ___ peeling of sugar cane
   ___ hospital equipment
   ___ other; specify:____________
   ___ don't know

44. After cutting the cord, what was applied:
   ___ string
   ___ medicine
   ___ nothing
   ___ tendon thread
   ___ hospital equipment
   ___ other; specify:____________________
   ___ don't know

45. What was applied on the cord during the first week of life?
   ___ string
   ___ medicine
   ___ nothing
   ___ oil
   ___ tendon (taami, fuwenda)
   ___ don't know
   ___ other; specify:____________________

______________________________________
CHILD

46. Child's bodyweight/size/height when born
   Bodyweight: Grams:__________  (twin Grams:_______)
   Size:     Big:______     (twin Big:______)
             Small:______ (twin Medium:______)
             Medium:______ (twin Small:______)
   Height: cm:__________  (twin cm:_______)

47. Did the baby cry within one minute after delivery? Y/N/U ___

48. Was the baby able to suck mother's milk just after birth?
   Yes:__  (twin Yes:___)
   No:__   (twin No:___)
   Didn't get chance:__  (twin Didn't get chance:___)
   Don't know:__        (twin Don't know:___)
   If No, or Didn't get chance, Why?:________________________

49. Did the infant stop sucking milk when he/she became ill? Y/N:__  (twin: Y/N:__)

50. In the first week (7 days) the baby got:
   Yes  No  Yes  No
   ___  ___ Mother's milk  (twin ___  ___)
   ___  ___ Cow's milk    (twin ___  ___)
   ___  ___ water        (twin ___  ___)
   ___  ___ porridge     (twin ___  ___)
   ___  ___ other;   (twin ___  ___) specify:_______
   ___  ___ don't know   (twin ___  ___)

51. Had the child been weaned before he/she became ill? Y/N:__
   If YES, how many months before death occurred? ___

52. Within the first month (30 days), the baby had:
   Yes  No  (twin Yes  No)
   ___  ___ Fever  (twin ___  ___) If YES, Explain:__________
   ___  ___ Diarrhoea (twin ___  ___) If YES, Explain:__________
   ___  ___ Cough   (twin ___  ___) If YES, Explain:__________
   ___  ___ Wasted  (twin ___  ___) If YES, Explain:__________
   ___  ___ Accident (twin ___  ___) If YES, Explain:__________
   ___  ___ Don't know (twin ___  ___)

53. How many days/weeks passed after birth before the infant became ill?_________

54. How did she get help when the child was ill? (Where, what kind of help, did it help?)
SYMPTOMS PRECEDING INFANT’S DEATH

Did the child have any of the following features during his/her last illness? If yes, indicate for how many days it lasted.

55.       Fever.............................  Y/N:__   Days:____
56.       Diarrhoea and/or vomiting........ Y/N:__   Days:____
57.       Cough and/or rapid respiration.... Y/N:__   Days:____
58.       Stiff neck...................... Y/N:__   Days:____
59.       Fits (convulsions).............. Y/N:__   Days:____
60.       Rash.............................. Y/N:__   Days:____
61.       Loss of weigh.................... Y/N:__   Days:____
62.       Drowsy or unconscious.......... Y/N:__   Days:____

If you obtain a positive answer to one or more of the above questions ask following questions (only ask about those features for which positive answers were obtained above).

FEVER

63. Was the fever __ very severe
    __ moderate
    __ mild

64. Was the fever __ present all the time
    __ intermittent

65. Was the fever the only feature of the illness? Y/N:__

DIARRHOEA AND/OR VOMITING

66. Did the child have sunken eyes? Y/N:__

67. Did the child have diarrhoea? Y/N:__
    If YES, 
    -was diarrhoea __ present throughout illness
    __ intermittent
    -was diarrhoea __ very severe
    __ moderate
    __ mild
    -when the diarrhoea was worst, how often did the child pass stool?
    __ <5 times per day
    __ 5-9 times per day
68. Did the stool ever contain blood? Y/N:__

69. Did the child have abdominal pain/colic? Y/N:__

70. Did the child have vomiting? Y/N:__
   If yes:
   - was the vomiting __ present throughout illness
     __ intermittent
   - was the vomiting __ very severe
     __ moderate
     __ mild
   - when the vomiting was worst, how often did the child vomit?
     __ less than 5 times per day
     __ 5-9 times per day
     __ 10 times or more per day

COUGH AND/OR RAPID RESPIRATION
71. Did the child have indrawings of the chest? Y/N:__

72. Did the child have wheezing? Y/N:__

73. Did the child have grunting respiration? Y/N:__

74. Was the child using alae nasi/playing nostrils? Y/N:__

75. Did the child have cough? Y/N:__
   If YES:
   - was cough __ very severe
     __ moderate
     __ mild
   - did the child cough up any sputum? Y/N:__
   - did the child cough up any blood? Y/N:__

76. Did the child have rapid breathing? Y/N:__
   If YES,
   - was breathing __ very rapid?
     __ moderately rapid?
STIFF NECK
77. Could the mother/guardian bend the neck of the child? Y/N: __

78. Does the mother/guardian think the child had meningitis? Y/N: __

FITS OR CONVULSIONS
79. How many fits did the child have?
   __ <5
   __ 5-9
   __ 10 or more

80. Were the fits __ small twitching?
    __ major movements?

81. Did the fits involve:
    __ face
    __ neck
    __ arms
    __ legs

82. Between fits was the child:
    __ fully awake
    __ drowsy
    __ unconscious

RASH
83. Was the rash present on the
    __ face
    __ neck
    __ arms
    __ palms
    __ legs

84. What were the features of the rash?
    __ flat patches
    __ bumps
    __ bumps with fluid
    __ bumps with pus
    __ other, describe: __________________________

85. Did the child have sore red eyes? Y/N: __
LOSS OF WEIGHT
86. Was the child thinner than he/she should have been? Y/N:__
   If YES, was the child thinner:
   ___ just during the final illness
   ___ since birth
   ___ since weaning
   ___ other, explain:_________________
87. Was the child shorter than he should have been? Y/N:__
   If YES,
   - had the child been smaller than usual since birth? Y/N:__
88. Did the child have normal appetite? Y/N:__
89. Did the child have swelling of the feet? Y/N:__
90. Did the child have flaky skin? Y/N:__

DROWSY OR UNCONSCIOUS
91. Was the child ___ fully awake?
   ___ drowsy?
   ___ unconscious?

FAMILY HISTORY
92. Were any other children in the compound seriously ill at the time that the child died? Y/N:__
   If YES, describe what kind of illness they had:_________________
93. Had any other children in the compound recently had measles?

RECORDS, HEALTH CARD
94. Can the child's health card be found? Y/N:__
   If NO, why? ______________________________
   Is Health card copied? Y/N:__
95. Are there any hospital records of child's illness? Y/N:__
   Are hospital records copied? Y/N:__

GENERAL COMMENTS
____________________________________________________________________

PROBABLE CAUSES OF DEATH
1. Main cause of death:______________________
2. Contributing:__________________________
3. Contributing:__________________________
4. Contributing:__________________________
5. Contributing:__________________________
### OBSTETRIC HISTORY

Previous pregnancies, first pregnancy no.1, second preg. no.2 and so on.

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<th>Year</th>
<th>Outcome: Months of pregnancy</th>
<th>Baby: Months of pregnancy</th>
<th>Sex</th>
<th>Lactating</th>
<th>Place of delivery</th>
<th>Place planned delivery</th>
<th>Who helped</th>
<th>Mode of delivery</th>
<th>Complications mother:</th>
<th>Child of death child</th>
<th>Cause of death child</th>
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8.4 RESEARCH PERMITS

**NEM**

DEN NASJONALE FORSKNINGSETiske KOMITE FOR MEDisin
Norges forskningsråd (NFR), avdeling NAVF

Bergen 3.10.94

Svend Gudmund Hinderaker
Senter for internasjonal helse
Armaker Hansen Building
5021 Bergen

**Prosjekt: BARNE- OG MØDREDGÆDELIGHEIT PÅ LANDSBYGDA I TANZANIA**

Det vises til din søknad av 5.08.94 til NEM samt brev av 20.09.94 fra Gunnar Kvale til NEM angående samme sak. Søknaden ble behandlet på NEM's møte 26.09. d.d. NEM har ingen kommentarer til prosjektet og tillår at det gjennomføres. NEM finner det ønskelig å få tilsendt en sluttrapport når prosjektet er blitt gjennomført.

Med hilsen

Jan Helge Solbakken
sekretariatsleder
TANZANIA COMMISSION FOR SCIENCE AND TECHNOLOGY

RESEARCH PERMIT

No.: 94-118 NA Issued: 14 June 1994

1. Name: Dr. Sven Gudmund Hinderaker

   From: Norway

   is hereby authorized to conduct research in Tanzania entitled as shown in 2 below.

2. Title: Perinatal and Infant Mortality and its Determinants in rural Tanzania.

3. Research shall be confined to the following region:
   Arusha region.

4. This permit is valid within the following date: from 14 June 1994 to 13 June 1995

5. Local contact/collaborator: Coordinator, MUTAN, KCMC, Moshi.

J.K. LIGUNDA (MrB)
for: DIRECTOR GENERAL

P.O. Box 4102 Dar es Salaam, Tanzania. Telephone: (032) 75311, 75312, 75314, 75315
Fax: (032) 75313
Email: dg@costech.wn.apc.org
TANZANIA COMMISSION FOR SCIENCE AND TECHNOLOGY

Telegram: COSTECH
Phone: 255 51 75311, 75312,
Director General's direct line: 74427
Fax: 255 51 75313
Telex: 41631 DEPLAN
E-M: costech@costech.gm.tz

In reply please quote:

Ref. No: Dr CST/RCA 94/23

14 June 1994

Director of Immigration Services
Ministry of Home Affairs
P.O. Box 512
Dar es Salaam

Dear Sir/Madam

RE: RESEARCH PERMIT

We wish to introduce to you Dr. Sven Gudmund Hinderaker from Norway

who has been granted research permit no. 94-118 NA dated 14 June 1994

The permit allows him/her to do research in the country entitled:

Perinatal and Infant Mortality and its Determinants in rural Tanzania.

Co-researchers, if any, are listed below.

We would like to support the application of the researcher(s) for the appropriate immigration status to enable the scholar(s) begin research as soon as possible.

By copy of this letter, we are requesting regional authorities and other relevant institutions to accord the researcher(s) all the necessary assistance. Similarly the designated local contact is requested to assist the researcher(s).

Yours faithfully

J.K. Ligunda (Mrs)
for: DIRECTOR GENERAL

cc: 1. Regional Development Director(s) Arusha region.
2. Local Contact
3. Other Institutions

Co-researchers
9 Research papers I-IV

Paper I: Perinatal mortality in rural Tanzania
Reproduced with the permission of Journal of Health, Population and Nutrition.

Paper II: Avoidable stillbirths and neonatal deaths in rural Tanzania

Paper III: Anemia in pregnancy in the highlands of Tanzania
Reproduced with the permission of Acta Obstetricia et Gynaecologica Scandinavica.

Paper IV: Anemia in pregnancy in rural Tanzania: Associations with micronutrients status and infections
Reproduced with the permission of European Journal of Clinical Nutrition.