

UNIVERSITY OF THE WITWATERSRAND

FACULTY OF HEALTH SCIENCES

SCHOOL OF PUBLIC HEALTH

RESEARCH REPORT

**TITLE: Clustering of mortality among children under five
Years due to malaria at the Ifakara Demographic
Surveillance Site in Tanzania.**

Mohamed Koblo Kamara

Research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg in partial fulfillment of the requirements for the Degree of Master of Science in Medicine in the field of Population Based Field Epidemiology.

Johannesburg, South Africa 2008.

DECLARATION

I, Mohamed Koblo Kamara declare that this research report work is my own work. It is being submitted for the degree of Master of Science in Medicine in the field of Population Based Field Epidemiology in the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University.

A handwritten signature in blue ink, enclosed within a light blue oval border. The signature appears to read 'Mohamed Kamara'.

Signature: _____

Full Name: Mohamed Koblo Kamara

_____7th day of November, 2008

Dedication:

This work is dedicated to the memory of my late father, Mr. Wusman Watson Kamara – may his soul rest in peace; and to the efforts of my lovely mother- Madam Isatu Fornah.

ABSTRACT

Introduction

Under-five mortality is still a major cause of concern in Sub Saharan Africa and among the highest in the world. This is also exacerbated by the high prevalence and episodes of malaria in this age group. The effect of detecting clustering of all cause and cause specific mortality and underlying factors is crucial for timely public health interventions. This is especially important for health authorities in Tanzania where under-five malaria attributable deaths accounts for 45% of the annual estimated mortality of 100, 000.

Study objectives

To estimate under-five mortality and analyze clustering of all cause and malaria specific mortality among under five children in Ifakara Demographic Surveillance System from 2002-2005.

Methods

Data from the Ifakara Health Research and Development Centre (IHRDC) were obtained for all under-five children who lived in 25 villages in the DSS from 2002 – 2005. Analyses for all cause and malaria cause specific under-five mortality were done using data collected from the DSS and verbal autopsy systems. Annual all cause and malaria specific mortality rates were calculated by dividing number of deaths and person years observed. Clustering of deaths for all cause and cause specific (malaria) in the 25 villages were analyzed using SaTScan™ version 7.0 software. A Poisson model was used to detect clusters with high rates in space and in space-time. Household assets and characteristics were used to construct a wealth index using Principal component analysis (PCA) in

Stata™ version9. The index was used to group households into five equal groups from poorest to least poor.

Results

Overall infants' mortality was sixty-three times higher (326 per 1,000 person years) compared to children (5.1 per 1,000 person years) and with mortality rates between girls and boys were very similar, (15.8 and 14.8 per 1,000 person years). Year of death and place of death (village) were found to be significantly associated with malaria deaths. However, socio-economic status of parents in households where deaths occurred was not associated to malaria deaths in the DSS. A number of statistically significant clusters of all cause and cause specific malaria deaths were identified in several locations in the DSS. The located clusters imply that villages within the clusters have an elevated risk of under-five deaths. A space-time cluster of four villages with radius of 15.91 km was discovered with the highest risk (RR 2.71; P-value 0.020) of malaria deaths in 2004.

Conclusion

These findings demonstrate that there is non-random clustering of both all cause and malaria cause specific mortality in the study area. The high infant mortality results also suggest a careful examination of the data collection procedures in the DSS and require further studies to understand this pattern of mortality among the under-five population. Appropriate health interventions aimed at reducing burden of malaria should be strengthened in this part of rural Tanzania. There is need to replicate this study to other areas in the country.

ACKNOWLEDGEMENT

I would like to acknowledge the support from, WHO/TDR for the award of this scholarship which enabled me to undertake this course in the School of Public Health at Wits. I am greatly indebted to them.

I would like to express my deepest thanks and appreciation to the Director and entire staff of Ifakara Health Research and Development Centre (IHRDC) for giving me an opportunity to use their data to write my research report and creating a suitable environment for my leadership training. Many thanks to my supervisors: Dr. Honorati Masanja of IHRDC and Mr. Edmore Marinda of School of Public Health, University of Witwatersrand for their supervision, guidance and support given to me throughout this research.

Special thanks to Dr. Tint, the academic coordinator for this course, Dr Ronell Kellerman for their support and guidance during my studies and to other lecturers at the School of Public Health, University of Witwatersrand.

I would also like to express profound thanks to Mrs. Lindy Mphahlele and Mr. Lawrence Mpinga for sorting out all administrative issues during the programme at Wits.

TABLE OF CONTENTS	Pages
Declaration	i
Dedication.....	ii
Abstract	iii
Acknowledgement.....	v
Table of contents.....	vi
List of Figures.....	ix
List of Tables.....	x
List of Acronyms.....	xi
List of Appendices.....	xiii

CHAPTER ONE

1.0 Literature Review	1
1.1 Introduction/ background.....	1
1.2 Problem statement.....	3
1.3 Study justification.....	4
1.4 Objectives.....	5
1.5 Review of Literature.....	6
1.5.1 Malaria burden and its impact on children under five years of age.....	6
1.5.2 Environmental factors attributable to clustering of malaria mortality.....	11
1.5.3 Socioeconomic factors attributable to spatial malaria mortality for under fives and resulting clustering of such deaths.....	12

CHAPTER TWO

2.0 Materials and Methods.....	15
2.1 Demographic Surveillance System and Study Area.....	15
2.2 Data collection.....	16
2.3 Exposure and Outcome.....	17
2.4 DSS Quality Control and Data Management.....	17

2.5 Verbal Autopsy.....	18
2.6 Determining Cause of Death by VA.....	18
2.7 Study Design.....	19
2.8 Study Population and Sampling.....	19
2.9 Sample Size.....	20
2.10 Data Management Procedures.....	20
2.11 Data Analysis.....	20
2.12 Ethical Consideration.....	23

CHAPTER THREE

3.0 Results.....	24
3.1 Socio-demographic and mortality characteristics of study participants.....	24
3.2 All-Cause under-five mortality estimates during four years of observation.....	25
3.3 Clustering of All-Cause under-five mortality during study period	28
3.4 Cause-Specific under-five mortality during four years of observation	30
3.5 Under-five malaria mortality during observation period in the DSA.....	33
3.6 Factors associated with cause-specific malaria under-five mortality.....	34
3.7 Clustering of under-five malaria mortality during observation period	37

CHAPTER FOUR

4.0 Discussion.....	40
4.1 All-cause under five mortality.....	40
4.2 Clustering of all-cause under-five mortality.....	42
4.3 Cause-specific mortality.....	43
4.4 Clustering of malaria cause-specific mortality.....	45
4.5 Limitations.....	47

CHAPTER FIVE

5.0 Conclusion and Recommendations.....	48
5.1 Conclusions.....	48
5.2 Recommendations.....	50

REFERENCE.....	52
APPENDIX.....	60

LIST OF FIGURES	Page
Figure 2.1 Map of the study area in the DSS.....	16
Figure 3.1 Kaplan-Meier survival estimates by age category.....	28
Figure 3.2 Major causes of under-five deaths in the DSS.....	32
Figure 3.3 Percentage of malaria under-five deaths by age category.....	33

LIST OF TABLES

Page

Table 3.1	Background demographic and mortality characteristics of study Participants.....	25
Table 3.2	Overall all cause under-five mortality estimates.....	27
Table 3.3	All cause under-five mortality clusters of spatial analysis.....	29
Table 3.4	All cause under-five mortality clusters of space-time analysis.....	29
Table 3.5	Specific major causes of under-five deaths by age group.....	31
Table 3.6	Univariate and multivariate hazard ratios models for factors associated with malaria mortality from 2002-2005.....	35
Table 3.7	Malaria under-five mortality clusters using purely spatial scan analysis	37
Table 3.8	Malaria under-five mortality clusters using purely space-time analysis	38

LIST OF ACRONYMS

CI	Confidence Interval
DIFD	Department For International Development
DSA	Demographic Surveillance Area
DSS	Demographic Surveillance System/Site
GIS	Geographic Information System
GPS	Geographic Positioning System
HR	Hazard Ratio
HRS	Household Registration System
ICD	International Classification of Diseases
IHRDC	Ifakara Health Research and Development Centre
INDEPTH	International Demographic Evaluation of Population and its Health Network
IRB	Institutional Review Board
MDG	Millennium Development Goal(s)
MOHSW	Ministry Of Health and Social Welfare (Tanzania)
PCA	Principal Component Analysis
RBM	Roll Back Malaria
RR	Relative Risk
SES	Socio Economic Status
SSA	Sub Sahara Africa
SQL	Structured Query Language
UNICEF	United Nations Children's Fund

VA	Verbal Autopsy
WHO	World Health Organization

APPENDIX

Appendix I.....Malaria Cause Specific Clusters in the study area during 2002-2005

CHAPTER ONE

1.0 GENERAL INTRODUCTION

1.1 BACKGROUND

Studies on spatial clustering and mapping of diseases particularly on communicable and parasitic diseases are increasingly becoming popular in raising public health awareness on disease burden and the risks they pose to the general population. This is in a way to establish spatial associations between potential risk factors of diseases and populations within a specified period of time either retrospectively or prospectively (Schellenberg et al., 1998; Gemperli et al., 2003; Balk et al., 2003; Andrade ALSS et al., 2004; Oesterholt et al., 2006; and Kazemba et al., 2006).

Malaria is one of the main parasitic killer diseases in Africa, particularly among the under five population. In recent years, the global incidence of malaria was estimated at three to five billion clinical cases annually, causing 2 to 3 million deaths each year (Breman et al, 2004). More than 90% of this malaria burden occurs in Sub Sahara Africa (SSA), where severe malaria episodes and deaths occur among children less than 5 years of age in rural and urban areas.

In SSA, it has been indicated that malaria tends to influence many childhood illnesses (all-cause). This crucial association has also been established to be the main indicator of under-5 mortality (McElroy, 2001). Children in this age group are those most likely to develop severe diseases and to be at risk of dying from malaria.

Against this back drop, the United Nations General Assembly adopted the Millennium Declaration which set what came to be known as the Millennium Development Goals (MDGs) to assist poor nations achieve basic bench marks for their development. MDG 4 aims to reduce child mortality by two-thirds by 2015 from a 1990 baseline (UNICEF, 2006).

However, meeting these goals has been a challenge to heavily malaria endemic countries like Tanzania, where annual clinical episodes of malaria are estimated at 16 million. Unfortunately, these episodes result in about 100,000 child deaths the majority of whom are from rural areas (MOHSW, 2002).

It is undoubtedly clear that the ever increasing body of knowledge on malaria research over the past decade ranging from incidence and transmission to risk factors and preventive measures and vaccine trials in localized areas in Tanzania and across SSA, has received enormous attention by health researchers. In complementing these efforts, clustering and mapping of malaria cases and mortality in particular presents an opportunity to providing vital clues in adequately informing public health authorities so as to provide immediate and timely intervention. However, detecting spatial clustering of malaria mortality can be better achieved in surveillance or monitored populations such as Demographic Surveillance Systems (DSSs) as demonstrated by this study.

The Ifakara Demographic Surveillance System is managed by the Ifakara Health Research and Demographic Center (IHRDC). The sentinel surveillance area is located in a rural area of Kilombero and Ulanga districts in the Morogoro region southeast

Tanzania. The districts like others are grappling with malaria episodes that are still causing havoc among under-five children. This has been a major concern for public health officials both at national and local levels. Currently, the DSS has an estimate population of 84,968 people, living in about 20,000 scattered rural households in 25 villages that are closely monitored (Ifakara DSS, 2007). Demographic data (births, deaths and migration) are periodically collected to estimate birth, death; in and out migration rates (INDEPTH Network, 2002). Mortality measurements due to specific causes including malaria are obtained using Verbal Autopsies (VA). These are interviews with surviving relatives on signs and symptoms that preceded death and are used to ascertain the probable cause of death (please see chapter 2; in sections 2.5 and 2.6 for detailed explanation). Even though efforts are made to document all-cause and cause-specific deaths, it is however clear that due attention has not been given to determine whether such deaths are clustered in one village, in one part of the demographic surveillance area (DSA) or are spatially distributed.

1.2 PROBLEM STATEMENT

Unlike the developed world, most developing countries are faced with huge challenges in dealing with epidemics such as malaria that are deeply entrenched in their communities. Malaria epidemics have resulted in loss of many lives particularly among children under five years old.

Extensive evidence has been generated on certain aspects of malaria research that have helped and guided the formulation of health policies in the country. There is still a need to obtain accurate data (figures) on both malaria episodes and deaths from different locations and determine if there is spatial clustering of such events. Studies on spatial

clustering of disease and their related attributes have provided vital information to health officials and have helped to reduce if not eliminate the risks they posed.

The DSS is one source of information on malaria attributed deaths at the population level and it can provide estimates for under-five deaths. Considerable attention has been paid in terms of regular and accurate data collection mechanisms on the health outcomes of the population. This provides an opportunity to study any possible spatial clustering of diseases either at community or village level in the DSA.

1.3 RATIONALE FOR STUDY

The challenging task to reduce the burden of malaria, in particular childhood morbidity and mortality, partly depends on accurate data on prevalence and incidence rates, death cases and where such events occurred. This is a problem in most rural communities where deaths sometimes go unreported and even those that are registered would certainly not reflect the true situation on the ground. Accurate figures on malaria deaths cannot be ascertained and hence making it impossible to determine trends, patterns and spatial clustering of such events in such settings.

Studies on spatial clustering of disease and their related attributes have provided vital information on trends, patterns and risk factors at community or village level to health officials who then hopefully determine appropriate interventions.

Sankoh et al. (2001) detected clustering of mortality in children younger than five years in Nouna demographic surveillance Area in Burkina Faso. The clusters reported do not

only raised the issue of childhood mortality but also served as a wake-up call for action. The novel idea of clustering of reported mortality events in a population especially among the under five, is to determine space (where) and time (when) those events (deaths) occurred and whether their occurrence was isolated to specific areas or are evenly distributed within the population. De Savigny and Wijeyarante (1995) have also emphasized its usefulness for health and the environment. Knowledge of the existence of clustering in the population is important for public health, as health authorities would be able to plan effective interventions. This study tested the hypothesis that there was no clustering of mortality cases among the under fives due to malaria at the Ifakara Demographic Surveillance Site.

1.4 STUDY OBJECTIVES

1.4.1 GENERAL OBJECTIVE

The general aim/objective of this study is to analyze clustering of deaths among under fives due to malaria at the Ifakara DSS (Tanzania) from 2002 to 2005.

1.4.2 SPECIFIC OBJECTIVES

1. To estimate the overall infant and under five mortality at Ifakara Demographic Surveillance System (DSS) from 2002 to 2005.
2. To analyze clustering of infant and under five deaths at village level at Ifakara DSS from 2002-2005.
3. To determine the proportion of deaths due to malaria among infants and under-fives at village level at the DSS.

4. To analyze clustering of malaria mortality for children under five at the Ifakara DSS from 2002 to 2005.

1.5 LITERATURE REVIEW

Clustering by way of definition refers to the non-random occurrence of a disease or mortality cases within an area over a succession of years (World Malaria Report, 2005). As Sub Saharan Africa (SSA) continues to bear the brunt of all malaria cases and deaths especially among its under-five population, it is imperative that clustering of malaria mortality can be adequately explained and understood if the burden and impact of malaria on the targeted group is known. In this regard, detailed assessment on the effect of environmental factors; (such as proximity to rivers, streams, dams, poorly drained areas and dwelling structures), climatic effects (i.e., assessing seasonal influence and temperature variability) across an endemic areas and socio-economic factors would be required to adequately explain the nature of clustering}.

1.5.1 Malaria burden and its impact on children less than five years

Globally, malaria is estimated to cause about 300 to 500 million clinical episodes causing over one million deaths annually. 60% of these episodes occur in Africa, South of the Sahara resulting in about one million deaths each year and children less than five years of age account for about 90% of these deaths (The Africa Malaria Report, 2003; WHO World Malaria Report, 2005). Most of these deaths occur in rural areas where access to drugs and prompt malaria treatment still remains poor. Increasing numbers of deaths attributable to malaria has continued to hamper successes made in decreasing under-five

mortality in SSA. Budgetary allocations to Health Ministries of various African countries are further posing very big challenges in their efforts aimed at reducing the malaria burden especially among under-five children.

With the high prevalence rate of malaria, governments and public health professionals in developing countries especially in SSA are increasingly worried with such trends and the challenges that lie ahead. There are a number of evolving strategies and initiatives which are being implemented by various health institutions in many African countries such as the Millennium Development Goals (MDG) and the Roll Back Malaria (RBM) which are geared towards reducing under-five mortality- highest in the world between 96-184 per 1000 live births by 2015 and 2010 respectively (DIFD Fact Sheet, 2005).

In 2000 and 2001, 17 countries in Africa south of the Sahara conducted surveys to determine their baseline situations with respect to rolling back malaria. Tanzania is one of the countries where RBM initiative has been factored into The National Malaria Control Program (NMCP) in a bid to strengthen the health system in its fight against malaria (World Malaria Report, 2005). In spite of efforts being made, malaria transmission is still considered to be endemic and has been the leading cause of death for children and adults. This situation has resulted in a steady increase in malaria reported cases from 7,489,890 in 2002 to 10,712,526 in 2003 with reported deaths of 14,156 in the later. In each case under five cases accounted for 45% of the reported episodes (3, 394,734 to 4, 800,768) (WHO World Malaria Report, 2005). Across Sub Saharan Africa fever and malaria are undistinguishable; however, the high fever prevalence is mostly attributed to malaria

which has been the main contributor to deaths among children under five years (A. Nicoll, 2000).

There are a number of factors that appear to have contributed to the resurgence of malaria: among the factors responsible are “changing rainfall patterns; water development projects such as dams and irrigation schemes, which create new mosquito breeding sites; adverse socioeconomic conditions leading to a much reduced health budget and gross inadequacy of funds for drugs; high birth rates leading to a rapid increase in the susceptible population under 5 years of age; and changes in the behavior of the vectors, particularly in biting habits, from indoor to outdoor biters” (WHO, 1996).

Environmental or ecological factors such as water bodies (dams, rivers and irrigation canals) have been reported to pose more risks to populations where they are found (Kazemba et al., 2006). In the same study on spatial variation of malaria risk in children aged 1–10 years in Malawi, Kazemba et al., (2006), used point-referenced prevalence of infection data to map out malaria risk areas. They showed high risk areas along water bodies such as lakeshore, Shire river valley and central plain areas, and the highlands having low risk. This has also been documented by other studies (Mabaso et al., 2005; Ghebreyesus et al., 2000). This in actual fact suggests that such high risk areas could possibly produce more malaria deaths than low risk areas.

Also, house design or dwelling type has also been recognized as a potential risk factor for mosquitoes’ attack on humans. Lindsay et al., (2003), found traditional houses with

simple ceilings designs reduce substantially the exposure to the malaria vector compared to those without. Charlwood et al (2003) discovered houses built in lower ground are more exposed to mosquitoes' attacks than those built on stilts. Despite the fact that both studies were conducted in distinct settings and with different methodologies, they however emphasize the fact that people living in sub-standard housing structures are continuously predisposed to the risk of malaria exposure. In such situations, malaria may be rife and can reach epidemic levels affecting the most vulnerable- the under five. This view was also supported by Gamage-Mendis et al., who observed in their study in southern Sri Lanka that incidence of malaria was strongly associated with the type of house construction irrespective of location. The risk was reportedly higher in inhabitants living in poorly constructed houses. This is especially true in rural areas where most people still remain very poor.

Most studies have reported an association between under-five mortality due to malaria and climatic risks factors such as season and temperature (Kynast-Wolf et al., 2002 and Kynast-Wolf et al, 2005). For example, in their study in Rural Burkina Faso, G. Kynast-Wolf et al., (2005), they investigated seasonal effect on mortality on children. They found a strong correlation between season and mortality especially at the end of the rainy season with increased risks during the dry season. The observed association was partly attributed to the high malaria mortality that occurred in the second stage of infancy in the area.

In addition to the already discussed factors, socio-economic status (SES) of the family is believed to be a potential risk factor on it own if it negatively impacts on the survival of

children. The determinants of socioeconomic status of child mortality are sometimes difficult to understand especially when relating them to the means of survival of their families (Blakely et al., 2003). Measurements of SES were initially based on the family's income, living standards and ability to spend money on health and other related activities. But this may not always be the case. In rural communities, variables normally considered in determining the SES of families vary from one region to another as well as on information on households.

McKenzie (2003) observes that income information does not capture the fact that other people especially the poor have income in kind that can be traded for such as durable assets and agricultural products. Standard economic measures of SES use monetary information, such as income or consumption expenditure being relatively uncommon in developed countries and limited data on child mortality by socioeconomic factors. The SES is a measure of individual or the family's living standard taken into consideration of educational background, access to water and electricity facilities, occupation or type of employment.

Others have used Principal Component Analysis (PCA) an approach which takes into consideration household assets of families in determining their wealth status in relation to others (Blakely et al., 2003 and Vyas et al, 2006). The aggregation of households assets in the PCA have been applied in other studies (Filmer and Pritchett, 2001; McKenzie et al., 2003) in developing a SES index, where households are grouped into quintiles to reflect different SES levels with their community.

From the various perspectives and approaches used by many researchers to associate under-five morbidity and mortality with environmental factors and socio-economic status

of parents or family, it is clear that such factors still pose a considerable threat on many childhood diseases including malaria. This further underscores the fact that malaria is a growing problem especially for the under-five children. It is also believed that there are many risk factors that predispose this vulnerable group to the disease (malaria) other than environmental factors and socio-economic status as highlighted above.

1.5.2 Establishing cause of death attributed to malaria

In the developing world, few countries have been able to put together estimates of cause-specific mortality rates that are sufficiently reliable (Mathers et al., 2005). In order to facilitate data collection on the health and socio-demographic characteristics of a population, the verbal autopsy protocol was developed as an alternative in the absence of other formal processes in rural communities.

Verbal Autopsy (VA) is an indirect way of assessing a cause of death and it largely depends on the basic knowledge of relatives of the deceased for “circumstances leading to the death” and recognizable signs and symptoms they could remember to determine a probable cause of death (Sibai et al., 2001; Kideit et al., 2005). Data on VA are generated through retrospective questioning in surveys which has been a common practice in DSS and is widely used in other situations to provide more information on most deaths whose causes are unknown.

This process is now becoming a standard way of establishing cause of deaths in many developing countries where statistics of those events are not available (Sibai et al., 2001). In Africa, most deaths are unattended or verified by health professionals, and information

on causes of death is generally incomplete. The situation is even worse in rural areas where they usually scratch for non-existent information. The use of VA in some rural parts across Africa is gradually increasing and forms the basis of establishing the cause of deaths in Demographic Surveillance Sites (DSS). (INDEPTH-Network, 2002).

This technique has been used by many studies in highlighting the burden of disease, cause of death and the pattern characterizing those events particularly among under-five populations (Sankoh et al., 2001; G. Kynast-Wolf et al., 2002; G. Kynast-Wolf et al, 2004; Gaudart et al., 2006 and Hammer et al., 2006). All these authors, have used VA in their studies conducted in rural Burkina Faso and have found under-five mortality due to malaria as the leading cause of death. Other studies conducted elsewhere have used similar approach to investigate cause of death and disease burden in their respective communities (Etard et al., 2004).

However, Sankoh et al., (2001) went a step further in his investigation and applied spatial analysis. This enabled him to look at spatial clustering of childhood mortality at village level. However, he failed to associate the mortality clusters to some specific underlying risk factors that are widely believed to increase the likelihood of a child dying from a particular cause of disease such as malaria.

1.5.3 Approaches to Disease Clustering

As the burden of malaria and other diseases are increasing in Africa, epidemiologists, researchers and public health professionals are also finding ambitious initiatives to limit the severity of their impact. These include among others surveillance and providing accurate, timely and up to-date data on disease burden, associated risk factors in a given

population. The focus has largely been on automated techniques such as statistical packages, which would assist in investigating and summarizing spatial data to establish spatial patterns of disease phenomenon in a population over time.

Apparently, a number of methods have been developed as potential approaches to enable researchers analyze data more rapidly, to predict disease risk areas, detect cases and clustering. This would inherently determine whether or not geographical relationships could be associated with observed phenomenon. Sankoh and Becher (2002) described a number of statistical techniques (software packages) used in cluster detection and analysis and stressed the fact that most can be adapted to several uses. They however cautioned that the selection of an appropriate test statistic suitable for a particular data set will certainly make more impact on one's results.

The spatial scan test (SaTScan) jointly developed by Martin Kulldorf based on the likelihood ratio test has been widely used for detecting geographical or spatial clusters using either the Poisson or Bernoulli model based scan statistics (Gaudart et al. 2006; Kulldorf et al., 1997). Both models have been used for the number of cases compared to the underlying population at risk such as disease mortality or incidence data. The Poisson model assumes that number of cases in each location is Poisson-distributed (Gaudart et al. 2006; Sankoh et al, 2001; Kulldorf et al., 1997). When there are no measurements of covariates, the expected number of cases in each area is proportional to its population size, or to the person-years in that area. Poisson data can be analyzed with the purely temporal, the purely spatial or the space-time scan statistic (Sankoh and Becher, 2002)

Cluster detection techniques using SaTScan were first used in cancer research (Kulldorf et al., 1995; Hjalmars et al., 1996 and Kulldorf et al., 1997) and have since then been introduced to other fields such as infectious diseases including malaria morbidity and mortality among children. Omumbo et al., (1998) used geographic information systems (GIS) to generate a map of malaria transmission intensity belt in Kenya and to predict malaria epidemics.

In a similar way, Sankoh et al (2001) incorporated GIS techniques with SaTScan to model for clustering of childhood mortality in rural Burkina Faso. The incorporation technique was aimed at producing maps of the study area using the output results of SaTScan. Measures such as mortality and morbidity rates are plotted on the map, thus showing areas of high or low rate.

CHAPTER TWO

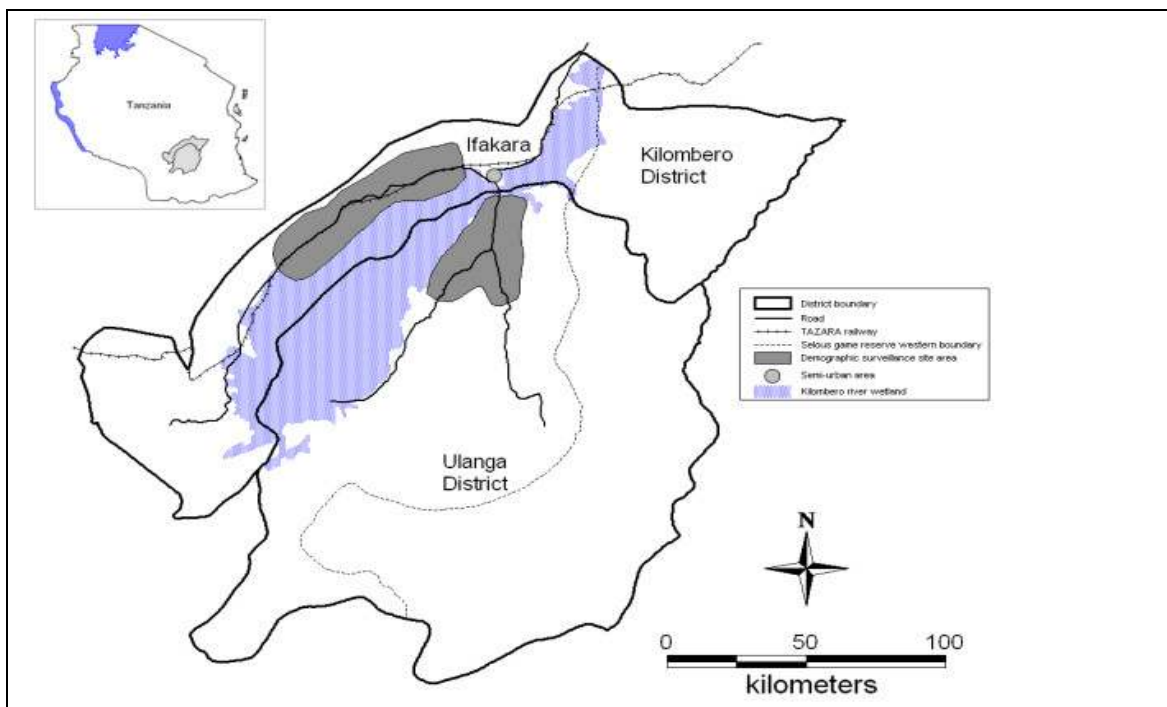
2.0 MATERIALS AND METHODS

2.1 DEMOGRAPHIC SURVEILLANCE SYSTEM AND STUDY AREA

The Demographic Surveillance System (DSS) is a structure of field operations where a defined population (individuals, households and residential units) in that DSA is followed up longitudinally to measure demographic and related health events. (INDEPTH-network, 2002). This is initiated with a baseline population census which defines the area and registers all the individuals living within that area.

The Ifakara DSS is a member of the INDEPTH-network which is an umbrella body that facilitates and coordinates some activities of member sites through a set of guidelines and also ensures that measurement tools are standardized and harmonized for all members.

The Ifakara DSS covers 25 villages (13 in Kilombero and 12 in Ulanga districts) in Morogoro region south-eastern of the country. It covers a land area of 80 km x 18 km in Kilombero district and 40 km x 25 km in Ulanga district, in all forming a land area of 2400 km² (INDEPTH-network, 2002; Hetzel et al., 2006). The two districts are divided by the extensive floodplains of the Kilombero River - a potentially high risk and malaria endemic area (see Figure 1). The DSS is predominantly rural with an ethnically heterogeneous population that practice subsistence farming, fishing and small scale trading (INDEPTH-network 2005, pp.35).



Source: Hetzel et al (2006).

Figure2.1: Map of Kilombero and Ulanga districts showing Ifakara town and the Demographic Surveillance System (DSS).

Malaria is the leading cause of death for the under-fives. As at March 2007, the total population of the DSS was about 82,000 with about 18,000 households.

2.2 DATA COLLECTION

This study used secondary data which were collected within the broader framework of the Ifakara DSS. Data collection is done once in every four months (DSS census rounds) to update the database – three times a year. This process precedes a baseline census that was conducted in 1997. Data on births, deaths and migration (in-migration and out-migration) were collected using an interview based questionnaire system and cause of

death determined through verbal autopsy. Data on the geo-reference location of each household was also collected at baseline but rarely updated.

For the purpose of this study, mortality data for all children under five years was obtained from the system's database and later classified into all cause and malaria specific deaths. In addition, the geo-reference location (co-ordinate) of each village within the DSS was collected using a hand held Geographic Positioning System (GPS) device. This was achieved by locating the central point of each village.

2.3 EXPOSURE AND OUTCOME

Measurements were categorized into exposure and outcome variables based on the available variables in the data. Exposure was determined by demographic such as age sex of study participants; and socio-economic factors such as, family assets, housing structure/type and parent or care giver's occupation. The socio-economic factors were later combined to compute the PCA to derive the SES component in the analysis. Outcome variables are all-cause and cause-specific mortality from where malaria deaths were obtained.

2.4 DSS QUALITY CONTROL AND DATA MANAGEMENT

The DSS has put a number of consistency checks in place to ensure that errors are minimized if not eradicated during data entry. Data from the field are received by filling clerks who then take appropriate inventory of them and later forwarded to data clerks for entries. The data are entered into Household Registration System (HRS)-a programme

specifically designed for DSS data management. This programme runs on Microsoft Fox-pro.

Inconsistencies detected by the system and data clerks are reported to the data manager who sends them back to the field for correction. Upon amendment, they follow the same channel and finally entered into the Household Registration System (HRS).

2.5 VERBAL AUTOPSY

Verbal Autopsy (VA) as briefly explained in chapter one, is an indirect way of assessing the probable cause of death of an individual. This process depends on information (basic knowledge) collected from relatives or close friends of the deceased for “circumstances leading to the death”. The information is based on recognizable signs and symptoms they can remember during the terminal illness to determine or ascribe a probable cause of death of the deceased. This is mainly used in DSS sites in developing countries and in other parts of the world, in an effort to put together comprehensive estimates of cause-specific mortality rates that are sufficiently reliable (Mathers et al., 2005; Kidek et al., 2005).

2.6 DETERMINING THE CAUSE OF DEATH

As an INDEPTH network member site, the Ifakara DSS determines cause of death by using an adapted version of INDEPTH-Network standard VA questionnaire. This is initiated by each census round or information received from key village informants on death event. An interviewer is then sent with a VA questionnaire to interview surviving relatives about cause, symptoms and duration of illness of the deceased. These forms are

sent to two (2) independent expert coders/reviewers (medical doctors) to assign cause of death with the aid of the International Scientific Classification of Diseases and Health Related Outcomes ICD-10.

Based on their reports, if they arrived at the same conclusion on a cause of death for a particular deceased person, their report will be documented as the “official” cause of death for that individual.

On the other hand, if the cause of death assigned was completely different for an individual(s), the form(s) will then be exchanged between them (to review for the second time) or sent to another reviewer (third reviewer) for assessment. In the later case, if the third reviewer arrived at a conclusion similar to one of the two reviewers, then, it is regarded as the final cause of death otherwise referred to as undetermined cause.

This system has so far worked well especially in research settings and resource poor countries (Philip W Setel et al., 2005; Mathers et al., 2005; Jean-François Etard Et al., 2004)

2.7 STUDY DESIGN

This study is a panel design using data generated from cross sectional surveys or census rounds (as described in the DSS) from 2002 to 2005. Data used for this study was collected prospectively in series of census rounds (3 each year) under the Ifakara DSS framework at Ifakara in Tanzania since 1997.

2.8 STUDY POPULATION AND SAMPLING

The study population which is the same as the sample size for all children younger than five years and all deaths in this age group recorded from 2002 to 2005 in the DSA.

2.9 SAMPLE SIZE

We used all deaths of children less than five years old that occurred in the DSA between 2002 and 2005. The sample size for this study is the total number of under-five children 29, 112 who are born and lived within the DSA during the study period (2002 - 2005). Still births were not included in estimates of deaths. Neonatal mortality form part of the mortality rates.

2.10 DATA MANAGEMENT PROCEDURES

All-cause mortality data for under-five for this study was extracted from the Ifakara DSS database using Structured Query Language (SQL) commands. Data cleaning was performed in Stata Version 9 where age and sex inconsistencies were identified and resolved by going back to the DSS databases and in some instances reference had to be made by checking original forms.

2.11 DATA ANALYSIS

The Household Registration System (HRS) programme was used for extraction of (all-cause and malaria-specific) mortality data for all villages in the Demographic Surveillance Area (DSA). The HRS is a custom designed programme written in Microsoft FoxPro that manages DSS data. The system can be used to estimate demographic rates (mortality and fertility) using person years or mid year populations as denominators.

Stata™ version 9 (Statistical and data analysis package) was used to carry out most of the analysis shown in this report. This included the construction of Principal Component Analysis (PCA), to estimate child mortality rates, and run regression models (univariate and multiple models) to investigate factors associated with child mortality.

We employed SaTScan™ version 7.0 software – a spatial epidemiological and statistical package designed for spatial and space-time statistical analysis that tests for clustering of diseases (e.g. malaria mortality) and related phenomenon (Kulldorff, 1997). This package has been found to be very useful by many researchers (Sankoh et al., 2001; Kulldorf et al., 1997; Hjalmars et al., 1996 Kulldorf and Nagarwalla, 1995) in determining the frequency or rate of occurrence and extent at which such events have occurred over a specified period of time within a defined area and population.

Since our outcome variable is the number of deaths, a Poisson model was adopted to estimate spatial clustering of child mortality rates that were later plotted on maps to show clustering.

The spatial model requires three specific files (case, population and coordinates) to be able to carry out the analysis. The case file comprised of village names or village IDs, cases (deaths), year, Age group and sex. Similarly, the population file is similar to the case file except that it contained person-years instead of cases (deaths).

The coordinate file comprised of village names, latitude and longitude locations of all the villages within the DSA. In the case and population files, the number of deaths by village and their associated person years were entered by sex and group (<12 months and 1yr-4yrs) for the study period - 2002 to 2005.

SaTScan evaluates mortality rates using circles in order to find the most likely or primary cluster and secondary cluster(s) with either a high or a low mortality rate. The most likely or primary cluster, a cluster of larger size would indicate areas of outstandingly low rates outside the circle rather than an area of exceptionally high rate within the circle. Areas in a circle signify areas of similar mortality levels. Different circles show area with different mortality levels. The reverse is the case when looking for clusters of low rates. The evaluated clusters are provided with information on circle radius, P-values, log likelihood ratio, risk estimation (for all data points and the corresponding number of observed cases, number of expected cases) and Relative Risk (RR) for each location. The estimated RR compares areas in terms of child mortality.

Finally, a standard Geographical Information System (GIS) programme – MapInfo Professional™ version 7.0 was used to translate the outputs into maps that depict clustering of all cause mortality as well as malaria specific deaths in the DSA for the observed period (2002-2005).

Social economic status was measured using a method proposed by Filmer & Pritchett. In brief, applying the Principal Component Analysis (PCA) in Stata™, households were categorized into five equal groups or quintiles based on household characteristics such as type of roof, walls, floor type and possession of assets e.g. radios, bicycles and animals.

Analyses were carried out for overall (all cause) and cause specific (malaria) mortality of under-five children for the DSS from 1st January 2002 to 31st December 2005 comparing age-groups (< 1yr and 1-4 yrs) and sex. Analysis for clustering of all cause mortality was

also performed to determine villages that are more at risk of under-five deaths. Cox proportional hazard regression methods were used to compare factors associated with under-five mortality. The Poisson regression model in SaTScan was used to scan the study area for clustering of all cause and malaria specific mortality.

2.12 ETHICAL CONSIDERATION

This is a secondary data analysis for which protocols were submitted for review. Ethics approvals were obtained from The Institutional Review Board (IRB) of Ifakara Health Research and Development Center (IHRDC) Ifakara, Tanzania (IHRDC/IRB/No.14-2006); and The Wits Ethics on Human Subjects Committee, University of Witwatersrand, Johannesburg, South Africa (M060902).

CHAPTER 3

3.0 RESULTS

Results of the analysis for this study are presented in two components. The first component of the analysis entails the estimation of overall (all cause) under-five mortality at the DSS from 1st January 2002 to 31st December 2005. Mortality rates in the study area were compiled for each year and compared by age-groups (< 1yr and 1-4 yrs), sex and SES with yearly totals.

The second component of the analysis looked at cause specific (malaria) mortality of under-five children from 1st January 2002 to 31st December 2005. Mortality estimates were compared by age-groups (< 1yr and 1-4 yrs) and sex with reference to year of death. Investigations for clustering of malaria specific mortality were performed to determine villages that are more likely at risk of under-five deaths.

3.1 Socio-demographic and mortality characteristics of study participants

A total of 29,112 children less than five years of age were included in this study from 1st January 2002 to 31st December 2005. There were a total 1,046 deaths of children in this age group registered during the same time period. For the purpose of this study, total population of children under-five years 29,112 was categorized into two age groups: infants (under 1 year) and children (1 – 4 years). Infants made up of approximately 16.6% (4,831) and children were 83.4% (24, 281). The mean age across the two age categories was approximately 3.1 years (37 months) CI (3.16, 3.20). Three quarters of all deaths were among infants.

There were almost equal number of males as females (14 556 (50%), 14 556 (50%) respectively). However, there were slightly more deaths (absolute count) among girls 539 (51.5%) compared to boys 507 (48.5%). Table 3.1 provides background information of study participants that are included in this study.

Table 3.1: Background demographic and mortality characteristics of study participants

Variable	Total Under 5 Pop		Total No. of Deaths	
Age category				
< 1 yr	4,831	16.6%	709	67.80%
1 - 4 yrs	24,281	83.4%	337	32.20%
(sub total)	29,112	100.00%	1,046	100.00%
Sex				
Female	14,556	50.00%	539	51.50%
Male	14,556	50.0%	507	48.5
(sub total)	29,112	100.00%	1,046	100.00%
Economic Status				
Poorest	2,940	10.1%	129	12.33%
Very Poor	3,361	11.55%	150	14.34%
Poor	3,612	12.41%	140	13.38%
Less Poor	3,751	12.88%	160	15.30%
Least Poor	3,484	11.97%	156	14.91%
Unknown	11,964	41.10%	311	29.73%
(sub total)	29,112		1,046	
Death Year				
2002	8,265		250	
2003	5,963		263	
2004	6,096		260	
2005	8,788		273	
(sub total)	29,112		1,046	

3.2 All cause under-five mortality estimates during four years of observation

A total of 1,046 under fives deaths and 68382.18 person years of observation were recorded during the four years of the study period. Overall under five mortality rate was

estimated at 15.1 deaths per 1,000 person years. Mortality rates between females and males were similar, 15.8 and 14.8 per 1,000 person years respectively.

However, there were wide variations in mortality rates. Infant mortality was sixty-three times higher 326 per 1,000 person years compared to 5.1 per 1,000 person years for children (please see Table 3.2 below). Table 3.2 summarizes the mortality rates by sex and age group and at village level in the study area with an overall estimate for the four years of observation.

Table 3.2: Overall all cause under-five mortality estimates during four years of follow-up

Variable	No of deaths	Person years	Mortality rate /000	95% CI	
Age category					
< 1yr	709	2176.684	326	303	350
1 - 4 yrs	337	66205.5	5.1	4.93	5.27
(sub total)	1046	68382.18			
Sex					
Female	539	34133.49	15.8	15.25	16.31
Male	507	34248.69	14.8	14.37	15.46
(sub total)	1046	68382.18	15.1	14.87	15.69
Village					
Idete (IDE)	57	4169.119	10.1	7.8	13.1
Idunda (IDU)	32	1602.633	41.1	10.5	20.9
Igima (IGI)	55	3376.734	12.1	9.2	15.7
Igota (IGO)	14	1159.433	8.9	5.3	15.2
Igumbiro (IGU)	29	1986.746	10.7	7.5	15.1
Ikule (IKU)	43	2106.073	15.1	11.2	20.4
Iragua (IRA)	34	3607.617	7	4.9	9.7
Kichangani (KIC)	46	2527.883	13.5	10.1	18
Kidugalo (KID)	36	2681.998	9.7	7.0	13.5
Kisegese (KIS)	22	1309.253	12.4	8.1	18.8
Kivukoni (KIV)	70	5140.299	10.1	8.0	12.7
Lukolongo (LUK)	49	3659.748	8.0	7.5	13.1
Lupiro (LUP)	64	3254.891	14.5	11.4	18.5
Mavimba (MAV)	27	2178.958	9.0	6.2	13.2
Mbingu (MBI)	92	5143.07	13.2	10.8	16.2
Mchombe (MCH)	60	4151.52	10.7	8.3	13.8
Milola (MIL)	10	1183.931	6.3	3.4	11.7
Minepa (MIN)	37	2136.277	12.6	9.11	17.4
Miwangani (MIW)	24	1673.303	10.6	7.1	15.8
Mkangawalo (MKA)	67	4630.609	10.7	8.5	13.7
Mngeta (MNG)	43	3110.435	10.2	7.6	13.8
Mpofu (MPO)	36	1938.287	13.8	9.92	19.1
Nakafula (NAK)	14	864.2861	10.7	7.1	17.7
Namwawala (NAM)	58	3112.453	13.7	10.6	17.7
Njagi (NJA)	27	1676.626	11.7	8.1	17.1
(Overall rate)	1,046	68382.18	15.1	14.87	15.69

From table 3.2 above, under-five mortality across the villages also varies greatly with some having higher rates compared to other.

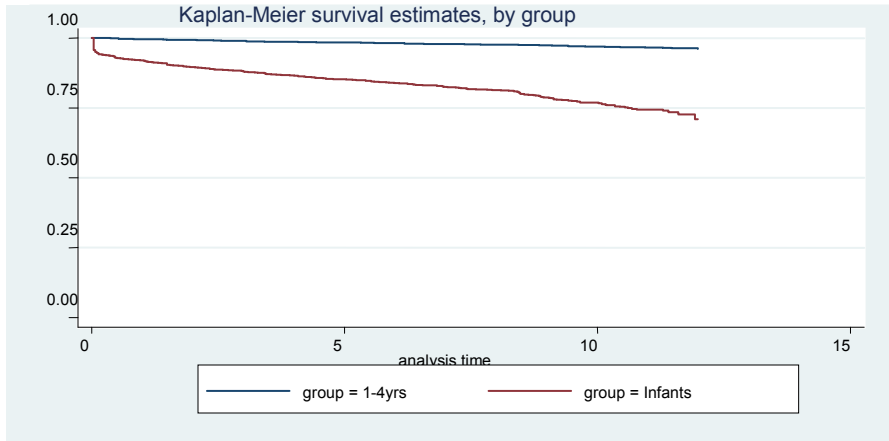


Figure 3.1: Kaplan-Meier Survival Estimates by Age Category

Log-rank test: $P < 0.001$

Figure 3.1 shows the Kaplan Meier survival curves by groups (group1 = represents children between age one and four years; and group 2 represents infants). The analysis time here is in months i.e. 12 months (One year), in this way we would be able to look at the effect of mortality on infants compared to children. Mortality among infants was higher (higher gradient), where 26% of infants had died by the end of twelve months. Survival in a one year follow-up period seems fairly improved for children between 1 and 5 years compared to under 1 year olds.

3.3 Clustering of all cause under-five mortality during observation period

The previous two tables above presented the background characteristics and mortality estimates for participants enrolled in this study. Those statistics only tell whether there are any differences between males and females on the one hand and age groups on the other. This sub-section therefore provides an insight on how such deaths were spatially distributed in the DSA. The tables below show two types of clusters detected and the total

number of villages found within each cluster and the relative risk (RR) associated with them.

Table 3.3: All cause under-five mortality clusters using spatial scan analysis

Cluster Type	Location	Circle Radius	Observed Cases	Expected Cases	Relative Risk	P- value
Most Likely	IKU, MKA, MNG, LUK, MCH, NJA, IGI, MPO, MBI, KIS	43.36 km	1049	920.16	1.264	0.001
Secondary	IDU, KIC, IGO, NAK, LUP	11.74 km	388	315.33	1.279	0.004

Table 3.4 provide results of the spatial scan analysis for all cause under-five mortality from 2002 – 2005. In this period, two types of clusters were detected. The most likely or primary cluster has a radius of 43.36 km with a P-value of 0.001. A total of nine villages were found in the cluster with an associated RR of 1.26. In the same way a significant secondary cluster (P-value 0.004) of five villages with radius of 11.74 km and RR of 1.28 was also detected. This implies that villages in those clusters were 1.26 and 1.28 times respectively more likely at risk of dying than those outside.

Table 3.4: All cause under-five mortality clusters using space-time scan analysis

Cluster Type	Location	Time Frame	Circle Radius	Observed Cases	Expected Cases	Relative Risk	P- value
Most Likely	NAM	2002/1/1 - 2002/12/31	0.018 km	22	170.34	0.120	0.001
Secondary	IKU,MKA, MNG,LUK,MCH, NJA,IGI, MPO,MBI, KIS	2002/1/1 - 2003/12/31	43.36 km	546	448.82	1.287	0.003

Similarly to the spatial scan analysis, the space-time also detected two significant clusters

(most likely or primary and secondary clusters) with P-values 0.001 and 0.003 and circle radii of 0.018 km and 43.36 km respectively.

Unlike the spatial scan analysis, the space-time provides a time frame during which a death cluster occurred. From table 3.4 above, both clusters started on 1st January 2002 but only the secondary cluster extended for a two year period to 31st December 2003. The villages detected in the most likely cluster using spatial scan analysis were also detected in the space-time in the secondary cluster with the same radius (43.36 km) and similar relative risks- RR 1.264 and 1.287 respectively. This implies that the identified clusters are ordered according to their likelihood ratio test statistic to determine a secondary cluster similar to a primary (most likely) cluster. The most likely cluster in the spatial-scan analysis having been evaluated was ordered as a secondary cluster in the space was-time.

3.4 Cause specific under-five mortality during four years of observation

The all-cause mortality does not present adequately by way of showing the proportions of all causes it entails for the observed period.

The cause specific mortality therefore provides a general breakdown to determine what proportion contributed by a particular specified cause of disease in the DSA. Table 3.6 below gives summary of major specific causes of under-five mortality for 2002 to 2005.

Table 3.5: Specific Major Causes of Under-five Deaths by Age-group and Year of death

Year of death	2002		2003		2004		2005		2002-2005	
Major Causes of death	Age-group		Age-group		Age-group		Age-group		Age-group	
	<1 Year	1-4 Years	<1 Year	1-4 Years	<1 Year	1-4 Years	<1 Year	1-4 Years	<1 Year	1-4 Years
Malaria	31	31	26	56	27	5	35	7	119 (27.36%)	99 (47.6%)
Pneumonia	22	3	16	16	10	0	12	0	60 (13.79%)	19 (9.13%)
Diarrhoeal Disease	4	2	4	4	3	0	3	0	14 (3.22%)	6 (2.88%)
Anaemia	1	1	5	3	4	4	5	5	15 (3.45%)	13 (6.25%)
Birth Injury	13	0	10	0	20	0	30	0	73 (16.78%)	0
Premature & low birth weight	8	0	12	0	17	0	11	0	48 (11.03%)	0
Undetermined	17	15	34	47	35	6	20	3	106 (24.37%)	71 (34.14%)
Yearly Total	96	52	107	126	116	15	116	15	435 (67.65%)	208 (32.35%)

Table 3.5 above shows the distribution of major causes of death in the DSS as categorized age-group and year of death. There are major observed differences in overall mortality between the two age categories- where infants accounted for 67.65% and children 32.35% of all major deaths as shown in the table. These differences are more evident when looking at yearly level. Malaria undoubtedly was found to be the leading cause of death for all the years (35%) with slight difference between age categories- infants 54.9% and children 45.4%.

Pneumonia was the second leading cause of death (12.3%) followed by birth injury related deaths with 11%. Like malaria, most of the deaths attributed to pneumonia (75.9%) occurred among infants. The graph below indicates the various proportions of major specific causes of death.

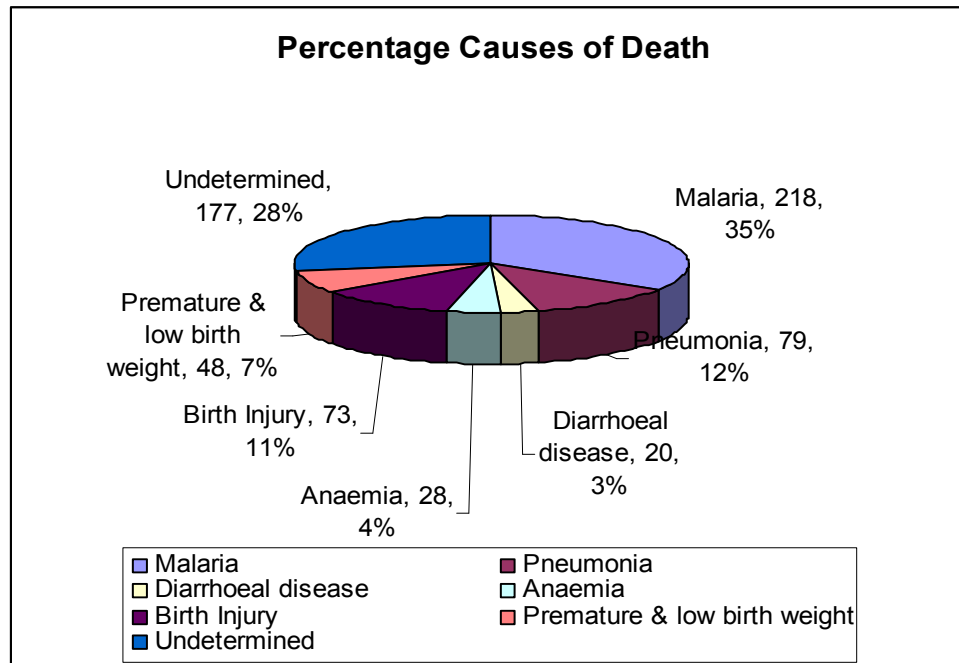


Figure 3.2: Major causes of Under-five deaths in the Ifakara DSA

Both the table and graph above have showed a high proportion of deaths that are categorized as undetermined (28%).

The classifications indicated in table 3.5 and figure 3.2 respectively above, show leading causes of death in children in the DSA. It is equally worth noting that instances where multiple causes of death were discovered, the most probable cause was then assigned to the particular death which therefore reflects the above scenario.

3.5 Under-five malaria mortality during observation period in DSA

Table 3.6 above, has already given us an overview on the distribution of some major cause of death including malaria. As one of the major contributors among deaths in

children below five years of age, malaria estimated mortality during the observed period was 35%, and has been the leading killer in each of the years. It shows yearly differences with 2003 and 2002 experienced the highest deaths 37.6% and 28.4% respectively followed by 2005 (19.3%) and 2004 (14.7%).

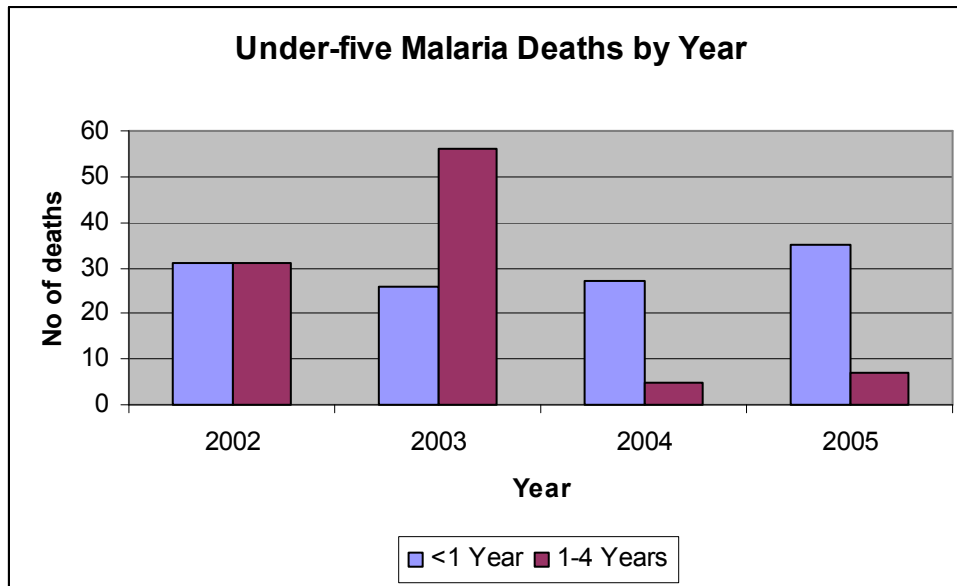


Figure 3.3: Percentage of Malaria Under-five deaths by Age group

The graph shows huge differences between age groups in 2003 (<1yr 31.7%, 1-4yrs 68.3%) 2004 (<1yr 84.4, 1-4yrs 15.6) and 2005 (<1yr 83.3, 1-4yrs 16.7%) respectively. On the other hand, there is no observed difference between age groups in 2002 as in the former.

3.6 Factors associated with under-five mortality due to malaria in the DSA

This subsection explores the relationship among factors that are closely associated with under-five mortality due to malaria in DSA from 2002 to 2005. Univariate and multivariate models were fitted to explore for associations with place of death, sex, age group and socio-economic status of households where the deaths occurred.

During the observation period from 1st January 2002 to 31st December 2005, a total of 29,112 children in the DSA were followed up in which 218 deaths attributable to malaria were determined by VA from a total of 1,046. The cause specific malaria mortality rate of 22.75 per 100 persons was also determined for the same period. Table 3.6 gives the RR for factors associated to under-five malaria deaths for both univariate and multivariate models below.

Table 3.6 Univariate and Multivariate Hazard Ratios (95% confidence intervals) models for factors associated with under-five malaria mortality from 2002 to 2005

Variable	No.	Univariate (unadjusted)			Multivariate (adjusted)		
		Hazard Ratio (HR)	P-value	95% CI	Hazard Ratio (HR)	P-value	95% CI
Sex							
Female *	539	-	-	-	-	-	-
Male	507	0.94	0.319	(0.83, 1.06)	1.05	0.97	(0.85, 1.09)
Age category							
<1 yr (infants)	782	46.6	<0.001	(38.7, 56.1)	46.9	<0.001	(38.9, 56.5)
1-4 yrs (children)*	264	-	-	-	-	-	-
Deathyr							
2002 *	250	-	-	-	-	-	-
2003	263	-	-	-	-	-	-
2004	260	1.3	0.003	(1.11, 1.64)	0.97	0.73	(0.80, 1.16)
2005	273	1.4	0.002	(1.12, 1.66)	0.81	0.036	(0.67, 0.99)
Socioeconomic status							
Poorest *	129	-	-	-	-	-	-
Very Poor	150	1.00	0.95	(0.80, 1.28)			
Poor	140	0.87	0.25	(0.68, 1.11)			
Less Poor	160	0.97	0.77	(0.76, 1.22)			
Least Poor	156	1.01	0.89	(0.81, 1.28)			
Village							
Idete *	57	-	-	-	-	-	-
Iunda	32	1.44	0.09	(0.94, 2.23)	1.29	0.24	(0.84, 1.99)
Igima	55	1.17	0.39	(0.81, 1.70)	1.05	0.81	(0.72, 1.52)
Igota	14	0.89	0.69	(0.50, 1.60)	0.89	0.71	(0.50, 1.61)
Igumbiro	29	1.09	0.69	(0.69, 1.71)	1.33	0.21	(0.85, 2.08)
Ikule	43	1.40	0.053	(0.99, 2.20)	1.39	0.10	(0.94, 2.07)
Iragua	34	0.69	0.08	(0.45, 1.05)	0.68	0.08	(0.44, 1.04)
Kichangani	46	1.37	0.12	(0.93, 2.02)	1.57	0.02	(1.07, 2.32)
Kidugalo	36	0.92	0.71	(0.61, 1.40)	0.92	0.71	(0.61, 1.40)
Kisegese	22	1.20	0.47	(0.73, 1.96)	1.12	0.65	(0.69, 1.83)
Kivukoni	70	1.02	0.90	(0.72, 1.45)	1.17	0.38	(0.82, 1.66)
Lukolongo	49	0.98	0.93	(0.67, 1.44)	1.00	0.98	(0.69, 1.47)
Lupiro	64	1.44	0.047	(1.01, 2.05)	1.44	0.04	(1.01, 2.06)
Mavimba	27	0.89	0.60	(0.56, 1.40)	0.91	0.68	(0.57, 1.43)
Mbingu	92	1.30	0.12	(0.94, 1.81)	1.29	0.13	(0.93, 1.80)
Mchombe	60	1.08	0.69	(0.75, 1.55)	1.25	0.23	(0.87, 1.80)
Milola	10	0.64	0.20	(0.33, 1.26)	0.73	0.36	(0.37, 1.43)
Minepa	37	1.21	0.37	(0.80, 1.83)	1.19	0.41	(0.79, 1.80)
Miwangani	24	1.06	0.82	(0.66, 1.70)	1.18	0.50	(0.73, 1.90)
Mkangawalo	67	1.08	0.68	(0.76, 1.54)	1.11	0.55	(0.78, 1.79)
Mngeta	43	1.02	0.91	(0.69, 1.52)	1.10	0.63	(0.74, 1.64)
Mpofu	36	1.34	0.18	(0.88, 2.03)	1.23	0.36	(0.80, 1.85)
Nakafula	14	1.22	0.51	(0.68, 2.18)	1.53	0.15	(0.85, 2.75)
Namwawala	58	1.34	0.12	(0.93, 1.93)	1.32	0.14	(0.92, 1.90)
Njagi	27	1.15	0.56	(0.73, 1.82)	1.24	0.35	(0.79, 1.96)

* Comparison group or Reference group

Age group (infants- less than 1 year; children- 1-4 years) was found to be associated with the risk of malaria deaths in the DSA. Children were less likely to die from malaria compared to infants, [unadjusted HR=46.6, P-value <0.001 95% CI (38.7, 56.1)]. After adjusting for the effects of sex, socio-economic status, place of death (Village) and year of death in the multivariate model, infants still had an increase risk of dying from malaria compared to children of 1- 4 years, [adjusted HR=46.9, P-value <0.001, 95% CI (38.9, 56.5)].

Some villages (place of death) were also associated to the risk of malaria deaths. For instance, Ikule and Lupiro were the only village significantly associated with malaria deaths with higher risk 1.44 [unadjusted HR=1.44, P-value 0.047, 95% CI (0.99, 2.20)] and 1.44 [unadjusted HR= 1.44, P-value 0.047, 95% CI (1.01, 2.05)] respectively. Adjusting for the effects of sex, age, socio-economic status, and year of death in the multivariate model, two villages namely, Kichangani and Lupiro, were found to be significant. Slight increase in risk for the former was detected and with no relative change in risk for the later [adjusted HR=1.57, P-value 0.02, 95% CI (1.07, 2.32)] and [adjusted HR=1.44, P-value 0.04, 95% CI (1.01, 2.06)] respectively.

Year of death was found to be associated with the risk of malaria deaths in the DSA. For 2004 and 2005 all children were less likely to die from malaria. After adjusting for the effects of Age group, sex, socio-economic status and place of death (Village) in the multivariate model, 2005 became significantly associated with malaria deaths compared to 2002, [adjusted HR=0.81, P-value <0.036, 95% CI (0.67, 0.99)]. However, the

association shows a decrease in risk compared to the reference period (2002). The decrease in risk for 2005 suggests a protective effect for that year. This phenomenon was investigated to determine whether there was interaction between year of death and other factors in the model. There is no interaction.

Univariate and multivariate results from the models for sex and socio-economic status show no association with malaria deaths in the DSS. This trend (no association) also persists after adjusting for the effect of other factors in the multivariate model.

Similar analyses were carried out using Poisson regression to determine whether the results obtained here may be different. The investigations revealed similar results.

3.7 Clustering of Under-five Malaria Mortality during observation period

Following the univariate and multivariate analysis of factors that are associated with malaria mortality, this subsection shows results of extended analysis of the Poisson regression model in SatScan to scan the study area for clustering of malaria deaths. The tables below show two types of analysis- spatial and space-time clustering.

Table 3.7: Malaria under-five mortality clusters using spatial scan analysis

Cluster Type	Location	Circle Radius	Observed Cases	Expected Cases	Relative Risk	P- value
Most Likely	IKU, MKA, MNG, LUK, MCH, NJA, IGI, MPO, MBI, KIS, NAM, IRA, KID	53.99 km	251	223.08	1.282	0.208
Secondary	(No cluster)					

Table 3.8 displays results based on the spatial scan analysis for under-five malaria mortality in the DSS from 1st January 2002 – 31st December 2005. The analysis only detected one cluster. The most likely cluster detected has a radius of 53.99 km with an associated RR of 1.28. However, P-value of 0.21 shows that the cluster lacks statistical significance. In the circle, there are 13 villages of which 10 were also detected in both the spatial and space-time analysis of all cause mortality in section 3.4. Though the circle was not significant, the RR of 1.28 shows that villages in the cluster are 1.28 times at risk of under-five malaria mortality than those found outside the cluster.

Table 3.8: Malaria under-five mortality clusters using space-time scan analysis

Cluster Type	Location	Time Frame	Circle Radius	Observed Cases	Expected Cases	Relative Risk	P- value
Most Likely	IKU, MKA, MNG, LUK	Jan-Dec 2004	15.91 km	21	7.97	2.713	0.020
Secondary	IGI, MPO, MBI, NJA	Jan 2002-Dec 2003	5.80 km	32	19.83	1.661	0.698

Unlike the spatial scan analysis, the most likely cluster detected in the space-time analysis above has a statistically significant P-value (0.020) with a higher RR 2.71. This cluster was detected in 2004 and consists of four villages with a circle radius of 15.91 km. This result is similar to the one obtained by univariate analysis that 2004 was the year with the highest under-five mortality risks in the DSA.

Also, the secondary cluster reported in table 3.8 above, occurred from 1st January 2002 to 31st December 2002 with a non significant P-value of 0.698. It also comprises of four villages that were also detected in previous clusters. The circle has a radius of 5.80 km with an associated RR of 1.66.

CHAPTER FOUR

4.0 DISCUSSION

Estimating all-cause under-five mortality and clustering of cause-specific deaths in rural areas of SSA has been made possible in a few countries in the sub-region where DSS sites exist that can provide timely and updated data collected at regular intervals within a year.

A number of studies have already been published on the pattern of all-cause childhood mortality in Tanzania (Bodker et al, 2003; Schellenberg D et al, 2004; TDHS, 2004/05 and Tottrup C, 2006). The Ifakara DSS in Tanzania has become a platform in which all-cause and cause-specific under-five mortality can be investigated using a standardized VA tool in rural areas of the country. This is the first study to report all-cause and cause-specific mortality childhood mortality and clustering of such deaths within the study area, using a VA method.

This chapter discusses results of all-cause and malaria specific under-five mortality and clustering of such deaths.

4.1 ALL-CAUSE UNDER-FIVE MORTALITY

The results of overall (all-cause) under-five mortality from 1st January 2002 to 31st December 2005 during the observation period shows huge difference between age categories. The death rate among infants is sixty-three times (326 per 1,000 person years) at 95% CI (303-350) compared to children (5.1 per 1,000 person years) at 95% CI (4.93-5.27). This pattern is consistent with other studies in the sub-region (McElroy et al.,

2001; TDHS, 2004/05 and Hammer et al., 2006). The observed high mortality rate in infants compared to children could partly be explained by other factors such as: gestational age of mother, educational level of parents, birth order, and HIV/AIDS status of parents which were not collected at baseline. However, other communicable diseases (including anaemia, pneumonia and malaria) may likely influence the high infant mortality rate. Most of these factors have been documented in several studies to either increase or decrease under-five mortality rates estimates proportionately.

The findings also show that mortality rate decreases gradually from age one to the age four years. This decreasing trend in mortality rate within children is comparable to findings of other studies conducted in the country (TDHS, 2004/05 and Tottrup C, 2006). In the DSA, the mortality rates for children younger than five years does not seem to show a gender difference between males 14.8 per 1000 person years and females 15.8 per 1000 person years. The total number of deaths among females was generally compared to males as indicated by the log rank test for sex (log-rank test for equality = 0.316). This is not consistent with results in the 2004-2005 Tanzania Demographic Health Survey, which shows a higher under-five (crude) mortality rate of 135 per 1000 in boys compared to 130 per 1000 in girls.

The results further reveal substantial differences in under-five-mortality rate among the 25 villages in the DSS. There are several villages that have higher mortality rates compared to others. The disparity in under-five mortality rate among villages would likely suggest that those with higher death rates may have certain underlying risks factors

that had contributed to such an outcome. However, among the most documented factors such as distance to the nearest health facility, access to medication, socio-economic status of the parent of household where access may be remote and not feasible for relatively poor households. In particular, lack of access to health facilities, and the alternative use of traditional medicine are obvious for increase or higher cause-specific village mortality (Schellenberg J.A et al., 1998).

4.2 CLUSTERING OF ALL-CAUSE UNDER-FIVE MORTALITY

The all-cause under-five mortality rates at village level indicates that systematic variations in all of the villages that made up the DSS in the study area. In an attempt to determine clustering of all-cause mortality, analyses based on the purely spatial and space-time probability Poisson regression were independently assessed as results shown in tables 3.3 and 3.4 demonstrate.

Both analyses reported an excess incidence in mortality among the 25 villages for the entire study period (2002-2005) with two statistically significant clusters for each. The primary (most likely) cluster in the purely spatial analysis comprised ten villages that cut across the two districts- Kilombero and Ulanga. The same ten villages were also detected in the secondary cluster of the space-time, with a similar radius of 43.36km and similar relative risk (RR) 1.26 and 1.29 respectively. The high relative risk associated with each of the clusters further confirms the high mortality rates estimated at village level. The results of the secondary cluster in the space-time, show a large size cluster, which only existed for a period of two years (1st January 2002- 31st December 2003). This result therefore reflects on the observed mortality at village level as indicated in table 3.1 (for years shown as being the highest in the study period).

Apparently, the secondary cluster in the purely spatial analysis had five villages from the two districts that are not in the two largest clusters detected in the spatial and space-time scan analyses for all cause under-five mortality. This cluster had an equally higher RR of 1.28 with a circle radius of 11.74 km compared to the most likely cluster in the space-time with a lower RR 0.12 and radius 0.018km and Namwawala (NAM being the village detected during 2002. These findings have shown a good match with results in table 3.2. This also suggests that the statistically significance results obtained for all-cause under-five mortality clusters detected in the study area could not have been by chance. Furthermore, results from these clusters are consistent with other studies in disease and mortality clustering (Onozuka D and Hagihara A, 2007; Sankoh et al., 2001).

4.3 CAUSE SPECIFIC MORTALITY

The Ifakara DSS like all others in the Sub-Saharan Africa and Asia is affected with deaths resulting from numerous conditions (Kynast-Wolf G et al., 2002; Etard J F et al., 2004; Hammer et al., 2006; Adjuik et al., 2006).

The cause-specific mortality results show that malaria, pneumonia, diarrhoeal disease, anaemia, birth injury and premature & low birth weight are among the leading killers of children under-five years of age in the DSA.

The malaria situation for infants does not seem to improve by the end of the study compared to children; this is due to an unprecedented surge in malaria deaths in 2005 after a steady decline in 2003 (26) and 2004 (27). In 2005, the overall infant deaths resulting from malaria (35) far exceeded the previous years and even surpass childhood deaths for that period. These trends of events are against the background of several

initiatives already implemented in collaboration between the Tanzanian government and its international partners to providing access to prompt treatment for children and pregnant women in the country.

The results also indicate pneumonia as the second major cause of death especially among infants relative to anaemia which claim more children's lives. Several studies have shown that, most deaths among under-five children are fuelled by malaria and in particular those classified as pneumonia and anaemia (Gemperli et al., 2003; Korenromp et al., 2004). It is likely that malaria may be a relevant risk factor for many deaths irrespective of the fact that it could not have been the immediate cause in the DSS.

Hence, it would have been important to also look at the relation of malaria endemicity to all-cause mortality as it is the case with its (malaria endemicity) relation to malaria-specific deaths.

In addition to anaemia and pneumonia, deaths due to birth injury and premature and low birth weight are important indicators and risk factors for infant mortality especially in malaria endemic regions (Steketee R W et al., 2001). He further asserts that, prematurity and intrauterine growth retardation resulting from malaria infection of the mother during pregnancy can be potential risk factors for maternal and infant mortality as well.

It is important that, results from this study should be interpreted with caution for the two districts considering the size of the DSS. However, due to the high numbers of malaria deaths and the pattern of deaths, one would suggest that malaria had largely influenced the observed trend in mortality in the DSS (Gemperli et al., 2003).

4.4 CLUSTERING OF MALARIA CAUSE SPECIFIC MORTALITY

In an attempt to determine clustering of malaria deaths, the results indicate three clusters of under-five deaths existed between 2002 to 2005. The spatial analysis detected the biggest/largest cluster with 13 villages (Ikule, Mkangawalo, Mngeta, Lukolongo, Mchombe, Njagi, Igima, Mpofu, Mbingu, Kisegese, Namwawala, Iragua and Kidugalo). The first eleven villages were also detected in the purely spatial and space-time analyses for all-cause mortality clustering as most likely (primary) clusters. Even though this cluster was not statistically significant, the high RR (1.28) seems to confirm the assertions given by Gemperli et al., (2003) and Korenromp et al., (2004) that all-cause mortality classified as pneumonia and anaemia in children below five years in most cases being influenced or caused by malaria.

In the space-time analysis; Ikule, Mkangawalo, Mngeta and Lupiro were detected in the most likely cluster which occurred from 1st January to 31st December in 2004. This cluster was statistically significant with the highest RR (2.71) in the study area with a circle radius of 15.91 km. The secondary cluster also detected four villages, like in the spatial, three of which have been detected in previous clusters. The secondary cluster was however not significant. The results indicate there were overlapping clusters of malaria deaths in the DSS from 2002 to 2005.

Importantly, the clustering results are very much consistent with results in the univariate and multivariate models for place of death (village) after adjusting for sex, age-group and socio-economic status. The villages found to be significantly associated with under-five malaria mortality were repeatedly detected in both the purely spatial and space-time

analyses for all-cause and malaria cause-specific deaths in the DSS. This may suggest that such villages could have certain underlying characteristics that predisposed them as being high risk to child mortality. These findings are similar to those observed in Nouna DSS (Burkina Faso) where certain villages were repeatedly found in clusters of all-cause childhood mortality (Sankoh et al., 2001).

In contrast to many studies, findings in this study show no association between deaths resulting from malaria to the socio-economics status of households where the deaths occurred. This could possibly be due to the close tie in proportion of households categorized in the various quintiles as indicated in table 3.1.

4.5 LIMITATIONS

Despite the compelling findings generated from this work, it's also worth noting that there were some limitations encountered during the conduct of this study.

To explore under-five mortality with other factors especially in a malaria endemic area, the need for key variables is essentially required. This work would have been more interesting if the relationship between malaria cause-specific deaths and variables such as mother's age and mother's educational level were examined to look for associations. These were not available in the data set by virtue of the fact that I use secondary data.

Also, the fact that was a panel-based design, retrospective data generated prior to the commencement of the study may not be entirely accurate and sufficient enough. This is because, VA data collection method relies on information given by surviving relatives; this would therefore raise recall bias issues which could affect the outcome of interest.

Finally, malaria diagnosis among children less than 12 months is difficult - may not be accurate as certain child illnesses such as pneumonia, anaemia and fever may tend to have the same symptoms like malaria and could therefore be classified as malaria.

CHAPTER FIVE

5.1 CONCLUSION

This study examined clustering of mortality among children under five years due to malaria at the Ifakara Health Research and Development Centre (IHRDC) Demographic Surveillance Site Ifakara, Tanzania. In an attempt to investigate clustering of under-five deaths, overall all-cause mortality rates were estimated by age category, sex and place of death (village). Univariate and multivariate Cox regression models were fitted to examine malaria cause-specific deaths with a defined age category, sex, socio-economic status of households, and year of death and place of death (village) for the period 2002 to 2005.

As anticipated, the death rate among infants was higher compared to children (1yr to 4 yrs) in the DSA. The results indicate an alarming mortality rate for infants - about six-three times higher relative to children. There have been a lot of evidences from other DSS that support this trend, but what seems different from this is the unusual high mortality rate among infants. The fact that the DSS is located in a predominantly rural area unlike others that are urban based or partly rural may have accounted for the observed huge difference in rate.

Mortality rate for girls was slightly higher in comparison to boys, which is also in contrast to studies conducted in other places. All these suggest an abnormal pattern that needs immediate attention to explain the phenomena.

Overall under-five mortality rates show geographical variation when examined at village level in the DSS. Villages with higher death rate are randomly located within the DSA

and this might be explained by certain underlying risk factors relative to their location. However, non spatial variations in under-five mortality rate at village level could more likely be determined by the presence or absence of a health facility that can be easily accessed.

Malaria, pneumonia, anaemia, premature and low birth weight and birth injury are the major leading causes of death in the 25 villages that make up the DSS.

There was no significant association between malaria cause-specific deaths and the socioeconomic status of family households where the deaths occurred. The absence of an association between malaria deaths and socioeconomic status could be ascribed to the wealth index that reflects on the sort of economic activities the people are engaged in. Being predominantly rural, the types of occupation in the DSS are subsistence farming, trading, and small scale cattle rearing.

Several malaria mortality clusters were detected. This clearly indicates that, there was clustering of death among children under-five years due to malaria in the DSS for the period 2002 to 2005. Villages detected in the most likely clusters to be at high risk of child death were also found to be significantly associated with deaths due to malaria in the multivariate model after adjusting for the effects of age-group, sex, socioeconomic status and year of death. The map showing clustering of all-cause and cause specific mortality also relates to the relative location of villages in the DSS.

In conclusion, this study has demonstrated that there are non-random pattern of clustering of all-cause and malaria cause-specific mortality. High-risk villages in terms of all cause deaths and malaria cause-specific deaths in particular were detected in the clusters. Hence, mapping of clusters of malaria-risk villages at the IHRDC DSA, will inform health authorities at both district and regional level for appropriate health interventions to be taken that will address the situation.

5.2 RECOMMENDATIONS

From the results, it has been noted that all- cause and malaria cause-specific deaths among under-five children is a cause for concern in the two districts that form the DSS. The findings of this study have implications for policy and planning, appropriate intervention programs and research.

Demographic Surveillance Sites in SSA are seen as a model in regular data collection exercise especially in rural areas. These procedures are expected to be standardized in a way to provide quality data. This study recommends that, the IHRDC should give extra attention to the field data collection and entry procedures in the DSS if the need for quality data was going to be maximized.

Cause of death (VA) data is very important for public health authorities to design appropriate health interventions. It is noted/ observed from the data that there are problems with the verbal autopsy data especially with the high proportion of undetermined cases. It is therefore recommended that thorough assessment in the way

VA data is obtained and classified in the DSS. This should entail additionally training for VA data collectors and coders especially in cases where they are not medical doctors.

Appropriate health interventions both at DSS and Local Administration level in the two districts should (go along side with short term plans-mentioned above) aimed at reducing common childhood diseases such as malaria, anaemia, pneumonia, that are shown to be the greatest killers of under-five children in the DSS in particular and in rural Tanzania in general.

As this is the first study that looks at clustering of mortality due to malaria among under-five children in the DSA, there is a need for further research to examine the pattern of under-five mortality rates observed. This must be accompanied by additional variables in addition to clustering techniques applied here. It is further recommended that similar studies be replicated to other areas in the country.

REFERENCES

Adjuik M, Smith T, Clarke S, Todd J, Garrib A, Kinfu Y, et al. Cause Specific mortality rates in sub-Saharan Africa and Bangladesh; *Bulletin of the World Health Organization* 2006; 84:181-188.

Balk, Deborah, Tom Pullum, Adam Storeygard, Fern Greenwell, and Melissa Neuman. 2003. *Spatial Analysis of Childhood Mortality in West Africa*. Calverton, Maryland, USA: ORC Macro and Center for International Earth Science Information Network (CIESIN), Columbia University.

Bodker R, Akida J, Shayo D, Kisinza W, Msangeni H A, Pedersen E M, et al. Relationship between altitude and intensity of malaria transmission in the Usambara Mountains, Tanzania. *Journal of Medical Entomology*; 2003 Sep; 40(5):706-17.

Brooker S, Clarke S, Njagi J K, Polack S, Mugo B, Estambale B, Muchiri E, Magnussen P and Cox J, 2004. Spatial clustering of malaria and associated risk factors during an epidemic in a highland area of western Kenya. *Tropical Medicine & International Health* 9 (7), 757–766.

Breman J. G, Alilio M. S and Mills A, 2004. Conquering the Intolerable Burden of Malaria: What's New, What's needed? *American Journal of Tropical Medicine and Hygiene*, 71(supplementary 2), 2004, pp. 1-15.

Charlwood J D, Pinto J, Ferrara P R, Sousa C A, Ferreira C , Gil V and do-Rosário V E, 2003. Raised houses reduce mosquito bites, *Malaria Journal*. **2** (2003), p. 45.

De Savigny D and Wijeyarante P, 1995. GIS for Health and the Environment. *International Development Research Centre (IDRC)*, Ottawa, Canada.

Etard J F, Hesran J Y, Diallo A, Diallo J P, Ndiaye J L and Delaunay V. Childhood mortality and probable causes of death using verbal autopsy in Niakhar, Senegal, 1989–2000. *International Journal of Epidemiology* 2004; 33:1286–1292

Filmer D, Pritchett LH. 2001. Estimating wealth effect without expenditure data – or tears: an application to educational enrollments in states of India. *Demography* 38: 115-32.

Gemperli A, Vounatsou P, Kleinschmidt I, Bagayoko M, Lengeler C, and Smith T, 2003. Spatial Patterns of Infant Mortality in Mali: The Effect of Malaria Endemicity. *American Journal of Epidemiology*; Vol. 159, No. 1.

Ghebreyesus T A, Haile M, Witten K H, Getachew A, Yohannes M, Lindsay S W, et al. Household risk factors for malaria among children in the Ethiopian highlands; *Transactions of the Royal Society of Tropical Medicine and Hygiene* (2000) 94, 17-21.

Ghebreyesus T A, Haile M, Witten K H, Getachew A, Yohannes A M, Yohannes M, et al. Incidence of malaria among children living near dams in northern Ethiopia: *Community based incidence survey*.

Hammer G. P, Somé F, Müller O, Wolf G.K, Kouyaté B and Becher H. Pattern of cause-specific childhood mortality in a malaria endemic area of Burkina Faso; *Malaria Journal* 2006, 5:47.

Hetzel M W, Msechu J J, Goodman C, Lengeler C, Obrist B, Kachur S P, et al.
Decreased availability of antimalarials in the private sector following the policy change from chloroquine to sulphadoxine-pyrimethamine in the Kilombero Valley, Tanzania; *Malaria Journal* 2006, 5:109 doi: 10.1186/1475-2875-5-109

Hjalmars U, Kulldorff M, Gustafsson G and Nagarwalla N, 1996. Childhood leukemia in Sweden: Using GIS and a spatial scan statistic for cluster detection. *Statistics in Medicine* 15, 707-715.

Ifakara Health Research and Development Centre DSS, 2007. *Unpublished Report on Quarterly Demographic and Health Surveys*, 2007.

INDEPTH Network, 2002. Population and Health in Developing Countries Monograph volume 1 (2002) -Population and Health at INDEPTH sites; International Development Research Centre (IDRC) PO Box 8500, Ottawa, ON, Canada K1G 3H9. <http://www.idrc.ca> [Accessed February 22, 2007].

INDEPTH Network, 2005. Measuring Health in Small Areas: Findings from Demographic Surveillance System. *Ashgate Publishing Limited*, 2005.

Kazemba L N, Kleinschmidt I, Holtz T H and Sharp B L. Spatial analysis and mapping of malaria risk in Malawi using point-referenced prevalence of infection data. *International Journal of Health Geographics* 2006, 5:41.

King G. and Lu Y, 2006. Verbal Autopsy Methods with Multiply Causes of Death

Korenromp E L, Armstrong-Schellenberg J R M, Williams B G, Nahlen B L and Snow R W, 2004. Impact of malaria control on childhood anaemia in Africa – a quantitative review *Tropical. Medicine and International Health* volume; 9 no 10 pp 1050–1065

Kulldorff M and Nagarwalla N, (1996). Spatial disease clusters: detection and inference. *Statistics in Medicine* 14, 799-810.

Kulldorff M. A spatial scan statistic. *Communications in Statistics – Theory and Methods* 1997; 26, 1481-1496.

Kulldorff M, and K, Gherman G, Williams G and DeFrancesco D. SaTScan Software for the spatial and space-time scan statistics, 1998. Version 2.1; Bethesda, Madison: National Cancer Institute.

Kynast-Wolf G, Sankoh O A, Gbangou A, Kouyate' B and Becher H. Mortality patterns, 1993–98, in a rural area of Burkina Faso, West Africa, based on the Nouna demographic surveillance system. *Tropical Medicine and International Health* 2002;

Volume 7 no 4 pp: 349–356.

Lulu K and Berhane Y. The use of simplified verbal autopsy in identifying causes of adult death in predominantly rural population in Ethiopia. *BioMed Central Public Health*. 2005; 5:58.

Mabaso M L H, Craig M, Vounatsou P, and Smith T. Towards empirical description of malaria seasonality in southern Africa: the example of Zimbabwe. *Tropical Medicine & International Health* 2005; 10 (9): 909–918.

Mathers C D, Fat D M, Inoue M, Rao C and Lopez A D. “Counting the dead and what they died from: an assessment of the global status of cause of death data.” *Bulleting of the World Health Organization Volume* 83(3, March); 2005: 171-177c.

McElroy P D, Terkuile F O, Hightower A W, Hawley W A, Phillips-Howard P A, Oloo A J, et al. All-Cause Mortality Among Young Children in Western Kenya. *The American Society of Tropical Medicine and Hygiene*, 64(1, 2) S, 2001, pp. 18–27.

McKenzie DJ. Measure inequality with asset indicators. BREAD Working Paper No. 042. Cambridge, MA: *Bureau for Research and Economic Analysis of Development, Center for International Development*, Harvard University. 2003;

Nicoll A. Integrated management of childhood illness in resource-poor countries: an initiative from the World Health Organization. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 2000, 94(1):9–11.

Omumbo J, Ouma J, Rapouda B, Craig M, Sueur D, Snow R W. Mapping malaria transmission intensity using geographic information systems: an example of Kenya. *Annual Tropical Medical Parasitology*. In press 1998.

Onozuka D, and Hagihara A. Geographic prediction of tuberculosis clusters in Fukuoka, Japan, using the space-time scan statistic. *BioMed Central Infectious Diseases* 2007, 7:26.

Roll Back Malaria Partnership, UNICEF and WHO/Malaria Department. World Malaria Report, 2005.

Sankoh O A, Ye Y, Sauerborn R, Mueller O, and Becher H, 2001. Clustering of Childhood Mortality in Rural Burkina Faso. *International Journal of Epidemiology*.30:485-492.

Sankoh O A and Becher H (2001). Comparison of Disease Cluster Detection Methods in Epidemiology with Application to Data on Childhood Mortality in Rural Burkina Faso,

West Africa. *Informatik, Biometries und Epidemiologie in Medizin und Biologie*. 32:264-275.

Schellenberg D, Menendez C, Aponte J, Guinovart C, Mshinda H, Tanner M and Alonso P. The changing epidemiology of malaria in Ifakara Town, Southern Tanzania. *Tropical Medicine and International Health* 2004; Volume 9 no 1 pp 68–76.

Schellenberg A J, Newell J N, Snow R W, Mung'ala V, Marsh K, Smith P G, et al. An analysis of the geographical distribution of severe malaria in children in Kilifi District, Kenya *International Journal of Epidemiology* 1998; 27: 323-329

Sibia A M., Fletcher A, Hills M and Campbell O. “Non Communicable disease mortality rates using verbal autopsy in a cohort of middle aged and older populations in Beirut during wartime, 1983-93.” *Journal of Epidemiology and Community Health* 2001; 55: 271-276.

Steketee RW, Nahlen BL, Parise ME, et al. The burden of malaria in pregnancy in malaria-endemic areas. *American Journal of Tropical Medicine and Hygiene* 2001; 64(supplementary):28–35.

Tanzania Demographic Health Survey, 2004-2005. Chapter eight: p5-6.

www.tbs.go.tz [Accessed 23rd June, 2007]

The United Kingdom's Department of International Fund for Development Fact Sheet, 2005.

Tottrup C, 2006. Geographical patterns of childhood mortality in Tanzania.

Short-term consultancy report for DANIDA Centre for International Health and Development University of Copenhagen & Institute of Geography University of Copenhagen; 2006.

Vyas S and Kumaranayake Y. Constructing socio-economic status indices: how to use principal component analysis Ghebreyesus et al. *Oxford University Press in association with The London School of Hygiene and Tropical Medicine*, 2006.

WHO/UNICEF World Malaria Report, 2005. The use of simplified verbal autopsy in identifying causes of adult death in predominantly rural population in Ethiopia.

Wolf G K, Hammer G P, Müller O, Kouyate B and Becher H. Season of death and birth predict patterns of mortality in Burkina Faso; *International Journal of Epidemiology* 2005; 35:427–435.

Oosterholt M J A M, Bousema J T, Mwerinde O K, Harris C, Lushino P, Masokoto A, Mwerinde H, Mosha F W, and Drakeley C J. Spatial and temporal variation in malaria transmission in a low endemicity area in northern Tanzania; *Malaria Journal* 2006, 5:98.

<http://www.malariajournal.com/content/5/1/98> [Accessed 12 April, 2007]

APPENDIX

APPENDIX: Malaria Cause Specific Clusters in the study area during 2002-2005

