Determinants of Time to Early Wean among Under Two years Children in Ethiopia; Application of Survival Models on EDHS 2016

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Determinants of Time to Early Wean among Under Two years Children in Ethiopia; Application of Survival Models on EDHS 2016

MSc Thesis

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STATEMENT OF AUTHOR

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As thesis advisors, we here by certify that we have read and evaluated the thesis prepared by **ObsaGuduru**under our guidance, which is entitled ***Determinants of Time to early Wean among under Two Years Children in Ethiopia; Application of Survival Analysis Models on EDHS 2016***

Based on our assessment, we recommend this thesis to be submitted as it fulfills the requirements of the final research for degree of Master of Science (MSc).

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External examiner_________________________ Signature __________Date _________

Internal examiner_________________________ Signature ___________Date _________

DEDICATION

This thesis is dedicated to my family especially to my lovely wife Nigist Kofi, my father in law Kofi Kabeto, my brother UshuGuduru and my friends who show me love and encourage me to back to school.

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Abstract

Background;Breast-feeding is a serious problem and yet it has more consequences for survival, health, productivity and intergenerational wellbeing in sub-Saharan country including Ethiopia. According to United National Development Program (UNDP) 2011 report 48% infants were not exclusive breast-fed in Ethiopia for the first six months age. In many countries including Ethiopia, exclusive breast feeding (EBF) practice is lower than the international recommendation. Thus, this study dealt with duration of breast-fed in Ethiopia based EDHS 2016 secondary data.

Objectives of the Study;The main objective of the study is to investigate the factors that shorten duration of Ethiopian children breast-fed and access duration of breast-fed variation across the regions by applying semi parametric shared frailty model on EHDS 2016.

Methodology; The data used for this study was the secondary data of the fourth Ethiopian Demographic and Health Survey (EDHS) of 2016 conducted by central statistical agency (CSA). The dependent variable of the study was the age in months at which children drop breast-fed. Semi parametric univariable frailty and multivariable shared semi parametric models analysis were applied in this study. When we use frailty models, θ is estimated to get an idea on heterogeneity/variation in the outcome between regions in this study. Expectation Maximization algorism (EM algorism) and penalized partial likelihood (PPL) parameter estimation technique were applied in this thesis.

Result and discussion; According to EDHS 2016Infants from Tigray and Amhara experienced more time breast-fed 92.34% and 92.26% respectively and Infants from Somali region experienced the least breast-fed duration which was 71.93% with 11 medians.Mothers age group, mothers work status, mothers visited by health worker in the 12 months and mothers visit were highly significant factors for early weaning time at $\alpha=0.05$ level of significance.

Conclusions;Maternal age were highly significant factor for early weaning time in Ethiopia; the government have to establish law for appropriate age for marriage probably beyond 25 years old. On the other hand pattern of contraceptive use was another significant factor for early weaning time; it recommended creating awareness in the community to expand using it (birth interval).

Key words; ***clusters, random effect, shared frailty model, time to wean, frail***

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Abbreviations

AFT	Accelerated Failure Time
AIC	Akaike's Information Criteria
BF	Breast-feeding
BLUEP	Best Linear unbiased Predictors
CDC	Centers of Disease Control and Prevention
CI	Confidence Interval
CSA	Central Statistical Agency
EA	Enumeration Area
EDHS	Ethiopian Demographic and Health Survey
ETR	Event time ratio
EBF	Exclusive Breast-feeding
FMOH	Federal Ministry of Health
HR	Hazard Ratio
IC	Information Criteria
LR	Likelihood Ratio
MLE	Maximum Likelihood Estimate/Estimator
REML	Restricted maximum likelihood
UNDP	United Nations Development Program
UNICEF	United Nation Children Fund
WHO	World Health Organization

CHAPTER ONE

INTRODUCTION

1.1 Background

Breast feeding can be defined as feeding the infants/babies human breast milk for some period since delivery[1–4].Breastfeeding plays very crucial role in reducing risk of getting ill or die/prevention of child from morbidity and mortality[1]. World Health Organization (WHO) and United Nation Children Fund (UNICEF) highly recommended exclusive breastfeeding for the first six months of age and continued breastfeeding at least 12 months or for 24 months [4].With increased breast feeding duration an estimated 820,000 children under the age of five could be prevented globally every year from dying [4]. According to United National Development Program (UNDP) 2011 report 48% infants were not exclusive breast-fed in Ethiopia for the first six months age[5]. Breast-feeding (BF) is incomparable way of providing the ideal food for the healthy growth and development of infants[6].

Previous paper on similar topic by MelkamuMolla and LeakemariamBerhe on EHDS 2005 used cox stratified regression modelswhich didn't accountunmeasured covariate[11]. Another study by; Laykewold etal (2017) on Exclusive Breastfeeding duration in Ethiopia used log-logistic regression which didn't account censoring and un measured covariates too [12]. Hence this thesis aimed to deal with such gaps too. Survival data is a term used for describe data that measure the time to a given event of interest with an assumption of the censoring time and the survival time are statistically independent random variables unlike logistic regression models [13]. While Cox's models assume the observations to be identically and independently distributed samples it doesn't account unmeasured covariates [14]. It is possible to perform survival analysis where there are unmeasured factors that may affect survival time as it is in this study casei.e. subjects may be exposed to different risk levels, even after controlling for known risk factors [15]. Hence, the data from a country like Ethiopia where there are diversities of nations and nationalities with different ethnic groups, cultures, languages and traditions practices needs special models that accounts those unmeasured covariates.

Such data type may be analyzed using shared frailty model.This is because some relevant covariates are often unavailable to the researcher or even unknown (Univariate frailty case)[16].

Frailty models are a fantastic and a good way to capture and to describe the dependence of observations within a cluster and/or the heterogeneity between clusters[17]. The specification of a frailty model is rather easy and frailty models are conditional models[18]. The frailty factor is a random and therefore a frailty distribution needs to be specified in the frailty model[19]. In this study the parametric baseline hazard function was unspecified. The cox stratified regression model is the optional model for frailty model when we use different and unspecified baseline hazard for each of the clusters [6]. The semi-parametric gamma frailty distribution and log-normal frailty distribution were used in this study.

Many studies used one parametric gamma frailty due to: (i) the choice of a gamma frailty make it possible to formally integrate out the frailties in the conditional survival likelihood resulting in an explicit and simple expression for the marginal likelihood.(ii) The choice of a parametric baseline hazard means that the marginal likelihood is fully parametric so that we can rely on classical maximum likelihood techniques to estimate the parameter [21].Ripatti and Palmgren showed that the penalized partial likelihood (PPL) can be treated as log likelihood, just as integrated full likelihoods can and this method used in this thesis[22]. For model selection AkakiInformation criteria (AIC), Bayesian information criteria (BIC) and I-likelihood value was used [14]].The Penalized Partial Likelihood (PPL) and the Expectation-Maximization (EM) Algorithm were used for parameter estimation [23, 24]. Restricted maximum likelihood (REML) was not used due to lack of a proper prior distribution for β [22]

The obtained data from Ethiopian Demographic and Survey (EDHS) 2016, aimed to explore the direct and indirect factor that determine the levels and trends of fertility and childhood mortality of the country. Based on this aim, the EDHS 2016 cross-sectional data collected on Infant and Young Child Feeding (IYCF) practices for all children born in the 24 months preceding the survey was used for this study [7]. The primary objectives of the study is to model Ethiopian children early weaning time using various semi-parametric shared frailties models and cox stratified regression model to identify the determinants and compare the semi-parametric frailty model output with the stratified model output. The multi stage stratified sampling technique was used for EDHS 2016 [7]. The event of interest in this study was the age at which children weaned from delivery in months. The R software of version 3.4.1 was used for all estimation through the study [8, 9].

1.2 Statements of the Problem

According to WHO and UNICEF exclusive breastfeeding for the first six month after delivery and continued breastfeeding for at least 12 months or upto 24 months[1, 2, 5] was highly recommended. Once malnutrition happens it is so challenge if not caught right at the beginning of a child's life (by properly breast-feeding) [25]. Breast-feeding is a serious problem and yet it has more consequences for survival, health, productivity and intergenerational wellbeing in sub-Saharan country including Ethiopia [1]. Since breast-fed lost before actual time is part of malnutrition it can be caused by numbers of factors such as income, illiteracy, belief in traditions, and place of residence in numbers of ways [11, 26, 27]Ethiopian Health and Demographic survey is one of the cross-sectional surveys conducted in Ethiopia within the interval of five years with numbers of key indicators to measures the levels of malnutrition in a country as a whole in addition to other health indicators [7].

According to United Nation Development Program (UNDP)the level of breastfeeding in developing world remained relatively constant over the years from 1995 through to 2010, only showing a 4% increase from 32% [28]. According to UNICEF report, early breastfeeding rates in sub-Saharan Africa have increased by 19% from 1995 to 2011[5]. This is the highest rate when compared to other regions. It is estimated that 41 % of children in sub-Saharan Africa are exclusively breastfed [29]. In many countries including Ethiopia, exclusive breast feeding (EBF) practice is lower than the international recommendation [29]. Studies conducted in Ethiopia indicated the different prevalence of exclusive breast-fed(EBF) in different areas of the country: EDHS 2005, 49%; EDHS 2011, 52%, with a mean duration of 4.2 months [29]. But still there is a long way to go as the country has high stunting rate. Evidence shows that the benefits of breastfeeding extend into adulthood [25, 30]. A well breastfed child has good sensory and cognitive development which is associated with better educational achievement[3]. Healthy and better educated children will be more productive and positively impact on socio-economic development[31].

The data with categorized variables and unmeasured variables result in discards of data and can be seen as introducing measurement error [22, 32]. It also leads to biased estimates and a reduced ability to detect real relationships. Omitting variables will simply reduce the predictive ability of a model, so that mothers with similar measured covariates will exhibit large variability in their survival[33]

Many of the studies conducted used logistic regression analysis and Cox proportional hazard models to estimate the effect of covariates on the early cessation of breast-fed /weaning time.The correct inference based on Cox's models needs identically and independently distributed samples and it restricts attention to the events that occur within the shortest time observed respectively[34]. Due to the following two reason Logistic regressions does not used and survival analysis instead; First survival analysis are usually a mixture of discrete and continuous data that require a different type of analysis than in the traditional discrete or continuous case[35]. The mixture is the result of censoring and has an important effect on data analysis. Second most evaluations are made conditionally on the knowledge available at the time of the analysis, and this change over time [35].

In Addition, the previous paper by MelkamuMolla and LeakemariamBerhe used the cox stratified model for similar data type which didn't account the variation across the regions [11]. Though it's constraint of not accounting the variation across the regionscoxstratified regression model wasapplied to saw the gaps regarding the determinants of early weaning factors. Often, the assumption of independent and identically distributed observations is violated.The shared frailty model was used with multivariable survival data where unobserved frailty is shared within groups of individuals[22, 36]. A shared frailty model may be thought of as a random effects model for survival dataand applied in this thesis to narrows the aforementioned problems.

This study claimed to answer the following questions;

- What aredemographic factors that determineearly cessation of breast-fed for Ethiopian children?
- Among gamma, Log t, and lognormal model which model best fits the Ethiopian children weaning data set?
- Investigating the variation of the weaning time ofEthiopia childrenacross the regions?
- Compare data output for shared frailty model and cox stratified model output in terms of their determinants significances and standard error (SE)?

1.3. Objectives of the Study

1.3.1. General Objective:

- The main objective of the study isto investigatethe factors that shorten duration of Ethiopian children breast-fed and access duration of breast-fed variation across regions by applying semi parametric shared frailty model.

1.3.2. Specific Objectives:

The specific objectives of the study:

- To identify the determinants factors which shorten the duration of Ethiopian children breast-fed.
- To investigate the random effect of time to early wean across the regionsof the country.
- To compare semi parametric shared frailty model output and cox stratified regression model with respect to identifying determinants factors.
- Compare the various semi-parametric shared frailty models that are used in modeling thedeterminants of early weaning for the data set.

1.4. Significance of the Study

The significances of the study are;

- Ethiopia is a country of nation and nationalities with different ethnic groups, cultures and traditions.Thus, it is difficult to ignore those variations for the analysis of data from such heterogeneous groups and this study enables the reader to know the variationof the weaning time of children across the regions of the country using selected models.
- Prolonging time to wean of Ethiopia children based on each categorical predictor.
- Policy and strategies designation for government and other stake holders.
- This study also help interested researcher in identifying which shared frailty distribution most appropriate from log-normal, Gaussian and gamma distribution?

- Further it may open door for interested researcher in this area for both nutritionist and statistician as it goes in both directions for further finding of determinant factors.
- In addition it helps to know the significance of variation of weaning time in different regions of the Ethiopia.

1.5. Ethical Consideration

The Research Ethics Review Board of Jimma University has provided an ethical clearance for the study. The author of this thesiswas granted to use the Ethiopian Demographic and health Survey of 2016 based on the permission got from the Demographic and Health Surveys (DHS) Program office. The data was sent through their very confidential email address for use.

CHAPTER TWO

2. LITERATURE REVIEW

2.1. Time to wean

Breastfeeding is the feeding of babies (of young children) with milk from a mother's breast[25]. It is also known as nursing. UNICEF and WHO Health recommended that breastfeeding to begin within the first hour of a baby's life and continue exclusively for the first six month age [31]. In the beginning few weeks of life babies may nurse roughly every two to three hours [25]. The duration of breast-feeding is usually ten to fifteen minutes on each breast[3]. For older children breast-fed is less frequently than infants. Pumping milk from mothers' breast can be used later when breastfeeding is not possible[3].

Breastfeeding provides mutual benefits for both mothers and infants, which any infant formula lacks for infants [4]. With increased breast feeding an estimated 820,000 children under the age of five could be prevented globally every year from dying [5]. Breastfeeding helps to decreases the risk of getting respiratory tract infections and diarrhea in both developing and developed countries[2]. Breast-feeding has also other benefits suchas lowering risks of asthma, food allergies, celiac disease, type diabetes, and leukemia[25]. Breastfeeding may also improve cognition abilities and decrease the risk of obesity/overweight in adulthood. Mothers may feel pressure to breastfeed, but in the developed world and capital cities of developing countries children generally grow up normally when bottle fed.

The benefits of breast-fed for the mothers are; less blood loss following delivery, better uterus shrinkage, and less postpartum depression[5]. It also delays the return of menstruation (might be used as delaying pregnancy naturally) and fertility, a phenomenon known as lactational amenorrhea. Breast–fed has also long term benefits for the mothers;it decreased risk of breast cancer, cardiovascular disease, and rheumatoid arthritis[37]. Breastfeeding is less expensive than infant formula. Health organizations, including the World Health Organization (WHO), recommend breastfeeding exclusively for six months and continue breast feeding for 24 months with supplementary food [5]. This means that no other foods or drinks other than possibly vitamin D are typically given for the first six months. After the introduction of foods at six months of age, recommendations include continued breastfeeding until at least one to two years of age. Globally about 38% of infants are only breastfed during their first six months of life. In the United States, about 75% of women begin breastfeeding and about 13% only breastfeed until the age of six months[5].

No medical conditions that do not allow breastfeeding.Mothers who take certain recreational drugs and medications should not breastfeed. Smoking, limited amounts of alcohol or coffee are not reasons to avoid breastfeeding. In an analysis of data on exclusive breast-fed (EBF) from 38 developing countries between 1990 and 2000 reported an increase EBF rate from 46% to 53% among infants younger than 4 months and from 34% to 39% for those younger than 6 months[3]. Higher increment was noted in urban areas (30% to 46%) than rural ones (42% to 48%). Although there were increases in all the regions studied viz. Middle East/ North Africa (29% to 34%), South Asia (49% to 56%), East Asia/Pacific (57% to 65%); the most impressive increment, however, was found in Sub Sahara Africa where the rate nearly doubled from 18% in 1990 to 38% in 2000[5].

In Ethiopia numbers of papers has been done especially on Exclusive breast-fed and respective factors associated with, thusthe overall rates of exclusive and full breastfeeding were 49.0% and 68.2% respectively in Ethiopia [12].According to that study; maternal education, marital status, wealth index and age of the child were closely associated with EBF practices by logistic regression model. Another study by MelkamuMolla and LeakemariamBerhe reveals that the mean and median duration of breastfeeding in Ethiopia were 25.64 and 24.00 months respectively[11]. They used cox stratified model and their analysis revealed that younger mothers, mothers who had lived in urban area, mothers having higher education, higher maternal parity, early pregnant and being a Muslim and protestant were significant determinants of early cessation of breastfeeding in Ethiopia[11].

Study in Australia by Scott JA, Aitkin I, Binns CW and Aroni RA revealed that maternal education, children gender, and mothers' work status were significant factor for exclusive breast-fed in that country using cox survival analysis [38]. Study in Iran conducted by Gholamreza .el found that maternal age were the significant predictive factors for time to wean in north Iran [39].The study conducted in Zimbabwe by MunjomaTakudzwa Pamela revealed that infant gender, Clinicians and health workers had an influential role in breastfeedinginitiation and continuation [38]. Antenatal attendance was a potential determinant of infant feeding practice [40–42].According to study in northern Iran the father's educational status and economic status did not have any correlation with either EBFD or BFD [43].

Another cross-sectional study in AnkeshaGuagusaWoreda, Awi Zone Northwest Ethiopia revealed that Maternal and paternal occupation, place of residence, postnatal counseling on exclusive breast-feeding, mode of delivery, andbirth order of the index infant were significant predictors of cessation of exclusive breast-feeding[44].

2.2Survival Analysis

The analysis of survival or other time to event data has played a key role in medical research done at Mayo Clinic since the clinic's earliest days[14]. In 1926, Gordon B New published an article titled "End Results of the Treatment of Malignant Tumor of the Antrum" in Proceedings of the Weekly Staff Meetings of the Mayo Clinic[19].An important concept introduced through these papers is the need to account for censoring when estimating survival rates[45]. Several medical manuscripts were subsequently published using this method, and the methodological work culminated in two papers with Robert R. Gage, and another member of the department. Lillian (Lila) Elveback joined the department in 1965 and added important practical and theoretical justification to the methods. Her guidance on how to lay out the tabular results and plots of a survival computation guided the early software in the department is still visible in the output of the R survival package and Mayo SAS macros[34].

Analysis of clinical data has continued to spur research in survival analysis. Methods for testing survival curves were contributed by Peter C. O'Brien; Thomas R. Fleming, Judith R. O'Fallon and David P. Harrington; and Daniel J. Schaid, H [19].Samuel (Sam) Wie and Terry M. Therneau.Methods and software for the comparison of observed survival for a cohort to what would be expected in the population at large, useful for the assessment of surgical cure, were developed by Kenneth P. Offord, Erik J. Bergstralh and others and later extended by Therneau (multiple HSR technical reports) [46].Diagnostic methods for survival models (e.g., functional form exploration) were explored by Therneau, Patricia M. Grambsch and Fleming, and by Cynthia S. Crowson, Elizabeth (Beth) J. Atkinson and Therneau. The addition of random effect terms to survival models has been explored by Daniel[36].

2.2.1 Definition and terminology of frailty Models

Shared frailty model can be defined as the extensions of cox model where the hazard function depends upon an unobservable random quantity that impact multiplicatively on it[47]. In the medical field frailty is a term that is used more frequently than it is defined[48]. The term generates from gerontology where it is used to rephrase that frail people have an increased risk for ill/morbidity and mortality/die [49].There is a common lack on how to determine the frailty status of an individual. A variety of tests have been generated to measure this status [49]. For instance a timed version of the “Get-Up and Go” (TAG) test; the test measures functional mobility for frail elderly people as the time that a patient needs to rise from an armchair, walk three meters, turn, walk back, and sit down again [50].

The frailty was first introduced by Vaupel in 1979 in order to interpret mortality data more appropriately as possible [51]. He was aimed to demonstrate that population mortality hazard rates do not reflect the mortality hazard rates of individuals from that population. Mortality rates for individuals typically increase rapidly with age than the observed mortality rate of the whole population. Consequently, Vaupel explained how mortality hazard rates changes. The idea of frailty provides a confortable way to introduce random effects in the model to account for association and unobserved heterogeneity[52]. The frailty model is a way of dealing with possible heterogeneity due to unobserved covariates or unmeasured covariates [45]. This is the main interpretation of frailty in the application to univariate time-to-event data analysis [53]

It is clear that most of the statistical models and methods for failure time data (and here especially the Cox proportional hazards model) were developed under the assumption that the observations from subjects are statistically independent of each other [34]. As this is sensible in many applications, it has become obvious that this assumption does not hold in other situations which are not as uncommon as originally thought [54].Beard (1959) proposes a two-parameter gamma distribution to model longevity, though I restrict my attention to a one-parameter gamma distribution with mean one and variance θ, which is the classical choice for the parameters when using gamma frailties.

Vaupel and Yashin (1985) show that caution is also needed in populations where unmeasured covariates are present through the existence of two subpopulations (where each subpopulation is assumed to be homogeneous or as the region in this study) [54]. It is somewhat different from using a frailty distribution to describe the heterogeneity present in the population[54]. They assume that each subpopulation has its own hazard function and demonstrate that the mixture of these two subpopulations can lead to quite unusual results at the population level. A frailty model is the model that becoming increasingly popular for modeling association between individual survival times within subgroups [54]. A frailty is an unobservable random effect shared by subjects within a subgroup. A frailty is sometimes called random intercept [55]. This most common model for the frailty is a common random effect that acts multiplicatively on the hazard rates of all subgroup/clusters members.

In this model, families with a large value of the frailty will experience the interested event at earlier times than families with small values of the random effect. Thus the most “frail” individuals will pass early and late survivors will tend to come from more robust families/in this study the most frail will loss breast-fed early. Frailty models can be used in making adjustments for over dispersion in univariate survival studies. The frailty represents the total effect on survival of the covariates not measured (not visible for researcher) when collecting information on individual subjects. If these effects are not considered, the resulting survival estimates may be wrong. Undertaking this dispersion effect in to account allow for adjustments for other unmeasured important effects. The shared frailty model is the most common model for frailty which is the extension of the proportional hazards regression model.

2.2.2. Some basic Frailty distribution functions

Numbers of suitable distributions have been proposed by statisticians so far, among them the gamma t, inverse Gaussian, log-normal, and power variancemodel are the commonly used distribution functions [51]. Of these distributions, the gamma has most readily been adopted in this research and in other applied research too as it is easily tractable [17]. One parametric gamma has some effect on the estimate effect of covariates, thus log-normal distribution function can be used as amending and others like inverse Gaussian and power variance can be used too[17].

2.2.2.1 The gamma distribution

The gamma distribution has been widely applied as a mixture distribution for instance Greenwood and Yule, Vaupel, Congdon, Santos and Hougaard as it can be easily integrated for parameter estimations [17]. From a computational and analytical point of view, it also fits very well to failure data. It is widely used due to mathematical tractability [34]. The conditional survival function of the gamma frailty distribution is given by Gutierrez [53]. For the Gamma distribution, the Kendall's Tau (Hougaard 2000), which measures the association between any two event times from the same cluster in the multivariate case[34].

Gamma frailty distribution has many applications in real world; Lancaster[56] suggested this model for the duration of unemployment. Another study by Andersenet al. used the gamma frailty model to check the proportional hazardsassumptions in his study of malignant melanoma. Vaupel et al., [51] also used the gamma distribution in their studies on population mortalitydata from Sweden

2.2.2.2 The lognormal distribution

This methodology first developed by McGilchrist for fitting frailty model that parallels the classical mixed models theory[19, 34, 53].The actual value of the random effect $W_i$which follows a zero-mean normal distribution with variance γ and the corresponding frailty has a lognormal distribution[17]. Although the lognormal frailty distribution is, for reasons discussed above, mathematically more complex, it has been used on a regular basis to fit frailty models[17]. Also in the context of accelerated failure time models one often assumes normal random effects.

CHAPTER THREE

3. Methodology

3.1. Weaning data set description

The secondary data source of the fourth cross-sectionalDemographic and Health Survey (DHS) 2016 conducted in Ethiopia by central statistical agency (CSA) was used for this study. The primary objective of the 2016 EDHS project was to provide up-to-date estimates of key demographic and health indicators[7]. Obtained data on child feeding practices, primarily breastfeeding was one of the key indicators which were dealt with under this study. The data was obtained from Demographic and Health Survey office based on requirement of the author after the DHS member ship was granted.

3.1.1 Sample Design

The sampling frame used for the 2016 EDHS was taken from the Ethiopia Population and Housing Census (PHC), conducted in 2007 by Ethiopian Central Statistical Agency (CSA)[57]. The census frame contained a complete list of 84,915 enumeration areas(EAs) created for the 2007 PHC. An EA is a geographic area covering 150 – 250 households.

The 2016 EDHS sampling technique was stratified and selected in two stages. Each region was stratified into urban and rural areas, yielding 21 sampling strata. Samples of EAs were selected independently in each stratum. In the first stage, a total of 645 EAs (202 EAs in urban areas and 443 EAs in rural areas) were selected with probability proportional to the EA size (based on the 2007 PHC) and with independent selection in each sampling stratum [7].In the second stage of selection, a fixed number of 28 households per cluster were selected with an equal probability systematic selection from the newly created household listing. Accordingly total of 18,008 households were selected for the sample, of which 17,067 were occupied (reached). Of the selected household 16,583 eligible women were identified for individual interviews and interviews were completed with 15,683 women [35]. Of the interviewed women all responses of mothers who had children age less than 24months were considered for this thesisi.e. mothers of 4242 children were included based on WHO and UNICEF recommendation for breast-fed duration. Thus, all children born in the 24 months preceding the survey was included for this study.

3.2. Variable Description

3.2.1 Dependent Variables

The dependent variable was the weaning time/ duration of breast-fed in months since delivery [11, 44, 57–59]. On a sample of all Ethiopian children age less than 24 months of EDHS 2016, it was retrospectively observed the timing to beginning of breast-fed until weaning time. It had to considered two things; first, all cases with no observed events are right censored. Therefore the children who had not yet experienced the event/time to wean of interest resulting in right censoring of the data. There is no reason for this censoring pattern to be dependent on the survival times and we consider it uninformative. Second, in order to make censoring valid, it has to assume that all children ceased breast-fed before the age of 24 months.

3.2.2. Independent Variables

The candidate covariates used in this studyare used by many researchers and institutions [11, 39, 44,57–59]

Table 1: Description of independent variableswith its categories and codes that are used for EDHS 2016 data set

Covariate name	Categories Description	Codes of covariates categories
Mothers age group	15-19	1
	20-24	2
	25-30	3
	30-34	4
	35-39	5
	40-44	6
	45-49	7

Wealth index	Poorest	1
	Poorer	2
	Middle	3
	Richer	4
	Richest	5
Place of current residence	Urban	1
	Rural	2
Religion	Orthodox	1
	Catholic	2
	Protestant	3
	Muslim	4
	Traditional	5
	Others	96
Education attained	No education	0
	Primary	1
	Secondary	2
	Higher	3
currently working	No	0
	Yes	1
Pattern of contraceptive use	Currently using	1
	Used since last birth	2
	Used before last birth	3
	Never used	4
Visited by health worker in the 12 months	No	0
	Yes	1
Antenatal care visit	No	0
	Yes	1
Husband Education status	No education	0
	Primary	1
	Secondary	2
	Higher	3

Children gender	Female	0
	Male	1

Mother's residential regions were considered as a clustering variable in all frailty models and stratum due to there were different ethnic groups with different languages, traditional practice, beliefs and cultures in each region. In the analysis mothers with age group of '15-19 years', poverty 'poorest', education 'no education' place of residence 'Urban', work status "not currently working" mothers religion "orthodox" pattern of current contraceptive use "currently using", visited by field worker "No", Antenatal care "No" ,gender of infants "female" and "no education" for husband education status which are coded '1, 1, 0, 0, 1, 1, 0, 0, 0 ,0 and 0'respectively were considered as the reference (baseline) indicator variables. Most of the covariates baseline references were based on mothers who didn't receive any inputs that improve their attitude/knowledge.

3.3. Method of Data Analysis

3.3.1 Survival Analysis

Survival analysis is the phrase used to describe the analysis of data in the form of times from a well-defined time origin until the occurrence of some particular event or end point[13, 14]. This time may be described in hours, in days, in months (in this study), or in years. It is also called the study of time to specific events (death, recovery from certain disease, cracking of certain building) [12].The main feature of survival data that renders standard methods not appropriate is that survival times are frequently censored [13, 46]. When the end points of the interest has not observed for individual in the studysuch survival time of individual is said to be censored[13].

Higher survival rate implies better treatment over other or better performance over other. In this study higher survival rate was implies longer breast-fed. In what follows, each uncensored observation is termed breast-fed dropout in this study regardless of whether breast-fed drop out or a event has occurred. Denote by T the random variable representing thesurvival time of children breast-fed. Let f(t), $t \geq 0$, denote the probability density function (pdf) of T (duration of breast-fed), andlet F(t) = P(T $\le$ t) = $\int_0^t f(t)dx$,t≥ 0 be the cumulative distribution function (cdf) of T. Thedistribution of T is called the survival time distribution or duration of breast-fed.The survival anaysis anticipates to estimate and to model the following;

- The survival function, S(t), defined as the probability that children breast-fed to time *t:*

$$S(t) = P(T>t) = \int_0^t f(t)dx = 1 - F(x),\ t \ge 0 \quad \ldots\ldots 3.1$$

- The hazard function, h(t), defined as the following ratio:

$$h(t) = f(t)/S(t),\quad t \ge 0 \ldots\ldots 3.2$$

It is interpreted as an instantaneous an instantaneous breast-fed lost in this study, since the probability that the event occurs within small time interval [t, t+dt], given that thesubject(breast-fed) to time t, t $\ge$ 0, is equal to:-

$$p\left(T < t + \Delta t \mid T > 0\right) = \frac{p(t \le T < t + \Delta t)}{p(T \ge t)} = \frac{f(t)}{S(t)}\partial t = h(t)\partial t \quad \ldots\ldots 3.3$$

- The cumulative hazard function, H(t), defined by,

$$H(t) = \int_0^t h(t)\partial\, t,\ t \ge 0 \quad \ldots\ldots 3.4$$

3.3.2 Non-Parametric Survival Analysis

It is better to consider non-parametric survival analyses first as it widely used in situations where there is doubt about the exact form of distribution. In survival analysis, the data are conveniently summarized through estimates of the survival function and hazard function. The estimation of the survival distribution provides estimates of descriptive statistics such as the median survival time. These methods are said to be non-parametric methods since they require no assumptions about the distribution of survival time. The Kaplan-Meier, Nelson-Aalen and Life Tables are the most widely used to estimate the survival and hazard functions [13].

3.3.2.1 Estimation of Survival function by the Kaplan-Meier Method

Kaplan Meier method is a widely used method for estimation of the survival function. This method produces the Kaplan-Meir estimatora nonparametric estimator, which does not assume any known algebraic form of the estimated survival function. The Kaplan-Meier estimator is also known as the KM estimator or the product-limit estimator. Suppose k distinct weaning times are observed. Arranged in ascending order, they are $t_1 < t_2 < .....t_k$ .At time t_i there are n_i children who are said to be at risk, those are survived up to this time (not including it) and were not censored. Denote by di the number of children who have an event at time t_i .To simplify notation, let $t_o = 0$ and $d_o = 0$; then the Kaplan-Meier estimator of the time to weanfunction S (t) is

$$\hat{S}(t) = \prod_{i:t \le ti} (1 - \frac{di}{ni}), t \ge 0 \ldots\ldots 3.5$$

Where d_i is number of events (breast-fed), and n_i is total number in the risks (all infants under age 24 months)

3.3.2.2 The Kaplan-Meier Survival Curve

The Kaplan-Meier survival curve is the plot of the Kaplan-Meier estimator of the survival function $\hat{S}$(t) against time t.This curve is a step-function that decreases at the times of events. The censored times (infants loss breast-fed) are usually marked by a cross (x). If an event and a censoring occur at the same time, a cross for the censored observation is put at the bottom of the step.

3.3.2.3 Median Survival Times

The Kaplan-Meier used to estimate fractals such as the median survival time. Consider the p^{th} fractal ξ p of the cumulative distribution function $F(t) = 1 - S(t)$, and assume that $F(t)$ has positive density $f(t) = F'(t) = -S'(t)$ in a neighborhood of ξ_p . Then, ξ_p is uniquely determined by the relations; $F(\xi_p) = p$ or equivalently $S(\xi_p) = 1 - p$. The Kaplan-Meier estimator is a step function and hence does not necessarily attain the value 1− p. Therefore a similar relation cannot be used to define the estimator ξ_{3p} of p^{th} fractals. Rather we define ξ_{3p} to be the smallest value of t for which (t) ≤ 1− p, that is, the time t where (t) jumps from a value greater than 1− p to a value less than or equal to 1− p. Hence the median survival times (ξ, 0.5) to be the smallest value of t for which (t) ≤ 0.5, that is, the time t where (t) jumps from a value greater than 0.5 to a value less than or equal to 0.5.

3.3.2.4 Log rank test

A common problem in survival analysis with categorical covariates is to compare two or more survivor functions, becauseof few statistical tests for such a comparison. The log rank test is in fact a chi-squared test for a large sample[60]. The log rank statistic compares the observed with an expected number of events[13]. The expected number of events is calculated by the method assuming that the null hypothesis is true. The null hypothesis assumes that the compared curves are the same. The comparison is performed at every time point the observed event occurred.

Testing H_0: There is no significant difference between the survival curves.

All goodness of fit tests shows significant difference in $s_{(t)}$ between two groups.

$$\log - Rank = \frac{\left(O_i - E_i\right)^2}{\operatorname{var}\left(O_i - E_i\right)} : \ \chi^2_{(1)} \quad \text{.........} 3.6$$

Where O_i is observed and E_i is expected value in group i.

3.3.3 Univariable frailty model

Frailty in survival analysis is the non-observable risks which are described by the mixture variables[34, 51, 53]. It is a random variable that is assumed to follow some distributional functions i.e. gamma, log-normal and etc.The hazard function of an individual depends on an unobservable, time-independent random variable U[53]. It acts multiplicatively on the baseline hazard function μ_o. Because of instability problems,a semiparametric estimation procedure basedon M-estimates and the EM algorithm is suggested. Frailty is assumed to be constant for each individual through time, but the composition of the population changes as time goes by[53]. The univariable frailty is a special case of survival model where there is only one time dependent covariate as fellows;

$\mu(t/X,U) = U\mu_o(t)e^{\beta' X}$ 3.7

,with $X = (X_1, X_2, ...X_k)$ and $\beta = (\beta_1, \beta_2, ..., \beta_k)$ as covariate and regression parameter, respectively. If it is standardized $E(U) = 1$ and variance $\sigma^2 = V(U)$ (if exist) and defined as measure of heterogeneity across the population in baseline risk.

3.3.4. The shared frailty model

A shared frailty model in survival analysis is defined as follows. Suppose there are *n* clusters and that the i^{th} cluster has n_i individuals and associates with an unobservedfrailty u_i $(1 \le i \le n_i)$. A vector x_{ij} $(1 \le i \le n_i, 1 \le j \le n_j)$ is associated with the ij^{th} complete survival time T_{ij} of the j^{th} individual in the i^{th} cluster. Conditional onfrailties U_i, the survival times are assumed to be independent and their hazard functionsto be of the form

$\lambda(t) = \lambda_{oj}(t)\exp(\beta^T X_{ij} + W_j) = U_i\lambda_{oj}(t)\exp(\beta^T X_{ij})$..................................3.8

Where $\lambda_{oj}(t)$ are the baseline hazard functions(no specified in this study), $U_i = \exp(W_s)$ (cluster effect/regions) and βare the regression coefficients associated with the covariate vector(education level, wealth index, mothers age group, religions, residence, mothers jobs) $X_{rsi} = (x_{rs1}, x_{rs2}, ..., x_{srp})x$ of length *p*. The frailties *Ui* are assumed to be identically and independently distributed random variables with a common density function *f* (*u; θ*), where *θ* is the parameter of the frailty distribution [36]. The assumption of a shared frailty model is that all individuals in all groups share the same frailty *U*, and this is why the model is called the shared frailty model [19]. All groups' lifetimes are assumed to be conditionally independent with respect to the shared (common) frailty.Conditionally on *U*, the hazard function of an individual in a pair is of the form $U\lambda o(t)$, where the value of *U* is common to all individuals in the group, and thus is the cause for dependence between life times within groups. Independence of the life times within a group corresponds to a degenerate frailty distribution (no variability in *U*). In all other cases, the dependence is positive. It is assumed that there is independence between different pairs. If P (*U* >0) = 1 holds, the shared frailty model leads to absolute continuous distributions and thus cannot model dependence due to common events. The standard assumption about the frailty distribution is that it is a gamma distribution with mean 1 and variance δ^2.The bivariate shared frailty model can be extended to the multivariate case with p related failure times, which results in the case of gamma distributed frailty in the following unconditional multivariate survival function:

$$S(t_1, t_2, ..., t_p) = \left(\sum_{i=1}^{p} (s_i(t_i)^{-\delta} - p + 1) \right)^{-\frac{1}{\delta}} \quad \text{3.9} \quad ,$$

Which was used for example by Cook and Johnson (1981) [22]. In the shared gamma frailty model with observed covariates the frailty U_i; (i = 1... n) in each clusters/regions can be estimated by [70]

$$U_i = \frac{\frac{1}{\delta^2} + \sum_{j=1}^{n_i} \delta_{ij}}{\frac{1}{\delta^2} + \sum_{j=1}^{ni} e^{\beta X_{ij} \lambda X_{ij}}} \quad \text{3.10}$$

This is possible because of the repeated observations in each cluster, where all observations in one cluster are based on the same value of the frailty variable.Asymptotic properties of the non-parametric maximum likelihood estimates in the shared gamma frailty model are well established. A graphical as well as a numerical method for checking the adequacy of the gamma distribution in a shared frailty model can be used [61].

3.3.4.1 Semi-parametricgamma frailty model

In the semiparametric frailty model, no assumption about the form of the baseline hazard function is made which requires new estimation strategiescompared to the parametric model[53]. Gamma distribution is widely used due to its mathematical tractability [61].It also has another two advantages as a frailty distribution[62]. First, the frailty distribution of the survivors atany given age is again a gamma distribution, with the same parameterand a different scale parameter. The second advantage is that thefrailty distribution among the persons weaning at any age is also agamma distribution, with the same shape parameter plus one, and ascale parameter as a function of the age at weaning time in this study.

In gamma frailty model, the restriction $\alpha = \lambda$ is used, which resultsin expectation of 1. The variance of the frailty variable can be then $1/\lambda$. Assumethat the frailty term U is distributed asgamma with $E(u)=1$ and $\text{var}(u)=\theta$. Then $\lambda=\alpha={}^{1}\!/_{\theta}$ The distribution function of the frailty term U is thenone parameter gamma distribution, u_i : $Gamma({}^{1}\!/_{\theta},{}^{1}\!/_{\theta})$;

$$g(u)=\frac{u^{\frac{1}{\theta}-1}\exp(-\frac{u}{\theta}),\theta}{\Gamma[\frac{1}{\theta}]\theta^{\frac{1}{\theta}}},\theta>0 \text{...} 3.11$$

With this frailty distribution, the mean of U is 1 and the variance is θ, so that large values of θ reflect a greater degree of heterogeneity among groups and a stronger association within groups. Similar to the parametric shared gamma frailty model, the unobserved frailty $Z_i=(i=1,2,3,...n)$ in each cluster can be estimated for semi parametric shared frailty model [63].Estimation for this model will held in the next section.

3.3.4.2 Semi parametric log-normal frailty model

This methodology developed for fitting frailty model that parallels the classical mixed models theory[34]. In most practical applications, the form of the underlying baseline hazard function is not known semiparametric models are preferred. If no assumptionsabout the form of the baseline hazard function aremade, parameter estimationbecomes much more difficult. One way to solve the estimation problem is the penalized partial likelihood approach discussed in the next section.The density of a normal distribution;

$$f_u(u)=\frac{1}{u\sqrt{2\Pi\gamma}}\exp(-\log u^2/2\gamma), \text{...} 3.12$$

With $\gamma>0$ The mean and variance of the frailty are given by; $E(u)=\exp(\frac{2}{\gamma})$ and $\text{var}(u)=\exp(2\gamma)-\exp(\gamma)$

3.3.5Stratified Proportional Hazards Models

Sometimes the assumptions of proportional hazard model can be violated for some covariates, as a result we use different and unspecified baseline hazard for each of the cluster. This gives the following semi-parametric stratified model;

$$h_{ij}(t) = h_{jo}(t)\exp(X_{ij}{}^{t}\beta)\text{.......}3.13$$

,With $h_{oj}(t)$ the baseline risk for cluster i (region i), in this model it assumed that the baseline hazards are completely unrelated nuisance functions and that the regression coefficients are the same in each stratum. Thus, this model is even more flexible than the fixed effects model as the baseline hazard can evolve independently over time within each cluster, whereas in the fixed effects model it is restricted to be of form $h_o(t)\exp(c_i)$ where c_i is the constant specific effect for cluster/regioni [37]. To estimate β we adapt the partial likelihood idea with

$$R_i(y_{ij}) = \{1 : y_{i1} \geq y_{ij}\}$$

The risk set for cluster i at time y_{ij} containing all the subjects in cluster i (region i) who are still at risk at time y_{ij} , the partial likelihood for this model is;

$$\prod_{i=1}^{s}\prod_{j=1}^{n_i}\left(\frac{\exp(x_{ij}{}^{t}\beta}{\sum_{l\in R_i(y_{ij})}\exp(x_{ij}{}^{t}\beta)}\right)^{\delta_{ij}}\text{.......}3.14$$

In this model a cluster contributes only if an event for a subject is observed while the other subject is still at risk.

3.3.6 Estimation in semi-parametric Cox PH model

When some author fit the Cox proportional hazards model, the author wishes to estimate the vector of regression coefficients, β[13]. This popular estimation approach was proposed by Cox (1972) in which a partial likelihood function that does not depend on $h_{o(t)}$ is obtained for β. Partial likelihood is a technique developed to make inference about the regression parameters in the presence of nuisance parameters ($h_{o(t)}$) the Cox PH model. In this section, the partial likelihood function was constructedbased on the proportional hazards model but cox stratified when not. Let be the observed survival time for *n* individuals. Let the ordered weaning/dying time of *r* individuals be

$t_{(1)} < t_{(2)} < \ldots < t_{(r)}$ and let $R_{(t(j))}$ be the risk set just before $t_{(j)}$ i.e. the group of individuals who are not weaned and uncensored (on breast-fed) at a time just prior to $t_{(j)}$. The conditional probability that the i^{th}individual dies/weaned in this study at $t_{(j)}$ given that one individual from the risk set on $R_{(t(j))}$ dies at $t_{(j)}$ is;

P (individual *i* weans at *t*(*j*)|one weaned from the risk set $R_{(t(j))}$ at *t*(*j*))

$$; \frac{\lim \Delta t \downarrow 0 P\{individualsweansatt_{(j)}(t_{(t)} + \Delta t) / \Delta t\}}{\lim \sum_{k \in R(t_{(j)})} P\{individualsweanatk(t_{(j)} + \Delta t)\} / \Delta t \Delta}$$

$$= \frac{\exp(\beta' x_{(i)}(t_{(j)}))}{\sum_{k \in R(t_{(j)})} \exp(\beta' x_{(k)}(t_{(j)}))} \qquad \ldots 3.15$$

Then, the partial likelihood function for the Cox PH model is given by;

$$l(\beta) = \sum_{j=1}^{r} \frac{\exp(\beta' x_i(t_{(j)}))}{\sum_{k \in R(t_{(j)})} \exp(\beta' x_{(k)}(t_{(j)}))} \qquad \ldots 3.16$$

in which $x_{(i)}(t_{(j)})$ is the vector of covariate values for individual *i* who weaned at $t_{(i)}$.

Note that this likelihood function is only for the uncensored individuals and this can extended easily for stratified cox model by multiplying its number of stratum. Let $t_1, t_2, \ldots t_n$ be the observed survival time for nindividuals and δ_i be the event indicator, which is zero if the i^{th} survival time is censored, and one otherwise. Then the above likelihood function can be expressed by;

$$l(\beta) = \prod_{i=1}^{n} [\frac{\exp(\beta' x_{(i)}(t_{(i)}))}{k \in R(t_{(i)}) \exp(\beta' x_{(k)}(t_{(i)}))}]^{\delta_i} \qquad \ldots 3.17$$

,where $R(t_{(i)})$ is the risk set at time $t_{(i)}$. The partial likelihood is valid when there are no ties in the dataset i.e. there are no two subjects who have the same event time.

3.3.7 Estimation in semi-parametric frailty models

3.3.7.1 The Expectation-Maximization (EM) Algorithm

The baseline hazard is unspecified and the frailties u_i are unobserved/not measured in the case of in a semi parametric approach [45].Therefore, it is difficult to maximize the likelihood to estimate the parameters. This kind of problem can be solved using the Expectation-Maximization (EM) algorithm which is typically used in the presence of unobserved (latent) information [64]. The EM algorithm iterates between the expectation and maximization step.

Expectation step; during this step the expected values of the unobserved/latent frailties conditional on the observed information and the current parameter estimates are obtained.

Maximization step; This is another step of expectation-maximization (EM) algorism where the expected values obtained in the E-step are considered to be the true information and new estimates of the parameters of interest are obtained by maximization of the likelihood, given the expected values. Its applicability for a particular problem depends on two conditions. First, it should be simple to obtain expected values for the unobserved/latent information. The second, the maximization of the likelihood, conditional on the expected values of the unobserved/latent information should be straightforward as the EM algorithm is based on performing these two steps iteratively. The execution of the EM algorithm is computer intensive and too slow**.**

3.3.7.2 The Penalized Partial Likelihood (PPL)

An alternative estimation method for EM algorithm is the Penalized Partial Likelihood (PPL) presented where the random effect is treated as a penalty term [46]. This method i.e. the PPL approach is preferred over EM algorithm due to its fastness and it is implemented in most standard software.

The PPL for normal random effects

The use of Penalized Partial likelihood (PPL) method for the lognormal frailty is motivated by the Laplace approximation to the full likelihood similar to the arguments used in the context of generalized linear mixed models [65]. The full likelihood is presented as follows;

$$l_{full}(h_o(.),\theta,\beta) = \log f(z,u / h_o(.),\theta,\beta) = l_{full,1}(h_o(.),\beta) + l_{full,2}(h_o(\theta)) \qquad 3.18$$

In PPL approach, $\log f(u/\theta)$ part of the likelihood is considered to be a penalty term such that if the actual value of the random effect (θ) is far away from its mean of zero, the absolute value of the logarithm of the density function evaluated at this value will be large and the penalty term has a large negative contribution to the full data log likelihood.Taking the random effects ($u_i^{'}s$)as another set of parameters in the first part of the likelihood, this likelihood part can be transformed into a partial likelihoodexpression as follows;

$$l_{ppl}(\theta,\beta,w) = l_{par}(\beta,w) - l_{pen}(\theta,w) \qquad 3.19$$

The first part $l_{pat}(\beta,w)$ is for the conditional likelihood of the data given the frailties, while the second part $l_{pen}(\theta,w)$ stands for the distribution of the frailties. Frailties are there in both parts of the penalized partial likelihood. On the other hand the second term penalizes random effects that are far away from the mean value zero (0) by reducing the penalized partial likelihood. This corresponds to shrinking the random effects towards the null-mean.

If $\eta_{ij} = x_{ij}^{\ t}\beta + w_i$ and $\eta_{ij} = (\eta_{11}, \eta_{12}, ...\eta_{cnc})$

$$l_{par}(\beta,w) = \sum_{i=1}^{G}\sum_{j=1}^{ni}\delta_{ij}[(\eta_{ij}\log(\sum\nolimits_{fw\in R_{(yij)}}\exp(\eta q w))]$$

$$l_{pen}(\theta,w) = \sum_{i=1}^{G}\log fW(w_i)$$

So for random effects w_i; i = 1…G (regions) with mean 0 normal density and variance θ i.e.

$$l_{pen} = \frac{1}{2}\sum_{i=1}^{G}(\frac{w_i^{\ 2}}{\theta} + \log(2\Pi\theta)) \qquad 3.20$$

Maximization in penalized partial likelihood approach is a double iterative process that alternates between an inner and an outer loop until convergence happens. Newton-Raphson procedure is used in the inner loop, to maximize, for a provisional value of β, θ and w, (best linear unbiased predictors, BLUPs [45]. For both gamma and lognormal frailty distributions, this step is identical.In the outer loop of a lognormal distribution, the restricted maximum likelihood estimator (REML) for θ is obtained using the best linear unbiased predictors, BLUPs.

Once the Newton-Raphson procedure convergence is reached for the value of $\theta^{(l)}$ a REML estimate for θ is given by

$$\theta^{(l+1)} = \frac{\sum_{i=1}^{G}(w_i^{(lk)})^2}{G-r} \qquad 3.21$$

Where $r = trace(v_{22})/\theta^{(l)}$ and G where number of stratums (regions). This outer loop is iterated until the absolute difference between two sequential values for $\theta, \| \theta^{(l)} - \theta^{(l-1)}) |$ is sufficiently small.

The penalized partial likelihood for the gamma frailty

The penalized partial likelihood (PPL) can be written in the similar way as for the normal random effects equation but with penalty function given by;

$$l_{pen}(\theta, w) = \frac{1}{\theta}\sum_{i=1}^{G}(w_i - \exp(w_i)) \qquad 3.22$$

Hence REML estimate is not available; the outer loop of a gamma frailty distribution is based on the maximization of a profiled version of marginal likelihood [45]. For gamma frailty model, PPL and EM algorithm lead to the same estimates but not for lognormal frailties.

3.3.8Heterogeneity parameter

Whenresearchers use frailty models, $\theta$is estimated to get an idea on heterogeneity/variation in the outcome between clusters/regions in this study. When θis large enough and differs significantly from zero; it shows heterogeneity between clusters/regions and a strong association among individuals in the same cluster/region. On the other hand, when θ is equal to zero, the frailties are identically equal to one which implies that the cluster effects are not present and events are independent within and across regions, which become same with marginal cox model [66]. The likelihood ratio test comparing the models with and without frailties is normally used for testing the null hypothesis θ= 0 ($H_{o;}$ θ=0)versus the alternative hypothesis θ>0 (H_1; θ>0). As the null hypothesis is at the boundary of the parameter space, a mixture of chi-square distribution with 0 and 1 ($\chi^2_{0,1}$) degree of freedom was used as suggested by Duchateau and Janssen[66].

3.3.9 Kendall's τ measures of dependence

Most of time dependence measures have been developed for bivariate data. It describesthe measures for such data. For two randomly chosen clusters *g (number of region)* and *k* of sizetwo, the event times are (T_{g1}; T_{g2}) and (T_{k1}; T_{k2}). The assumption is that thecovariate informationcannot change in each cluster/region. Kendall's τ is a global measure of dependence and is definedas;

$$\tau = E[sign((T_{g1} - T_{k1})(T_{g2} - T_{k2}))] \qquad 3.23$$

Where $sign(x) = -1, 0, 1$ for $x < 0$, $x = 0$, $x > 0$.

3.5 Model Diagnosis

3.5.1 Schoenfeld residuals

When the author return to the Cox proportional hazard model, he will consider eponymous residuals due to (Schoenfeld, 1982) that are centered on zero and should be independent of time if the proportional hazard assumption is true [13, 14]. Different from this, i.e. residuals that exhibit some trend in time indicate that the proportional hazard assumption is violated. Thus, researcher can perform a formal test of this hypothesis for identifications'. The proportional hazard assumption can never be merely fails to reject it (as with all classical hypothesis testing: though Bayesian hypothesis testing is different) [14].

The approach considers one covariate at a time that is one set of residuals and one p-value per covariate in the model and it can be extended to the multivariate case too. To make it too simple, it is possible to start with the case where there is only one covariate in the model. Recall that at any instant in time t, if a failure were to occur and the model were correct, the failure would happen to individual k with probability;

$$p(k, fail) = \frac{e^{\beta x_k}}{\sum_{j \in R\{t\}} e^{\beta x_j}} \qquad 3.25$$

The individual who fails at time t_i has covariate x_i. The expected value of this is;

$$E(X_i) = \frac{\sum_{k \in R\{t_i\}} x_k e^{\beta X_k}}{\sum_{j \in R\{t_i\}} e^{\beta x_k}} \qquad 3.26$$

And so the difference between the observed and expected covariate of the person who fails at time t_i is;

$$\hat{r} = x_{i-} \frac{\sum_{k \in R\{t_i\}} x_k e^{\beta x_k}}{\sum_{j \in R\{t\}} e^{\beta x_j}} \qquad 3.27$$

Clearly this has expected value zero (if the proportional assumption is true). It should also be independent of time if the proportional hazard assumption is true. The same approach applies to models with more than one covariate.

3.6. Comparison of Models

Model comparison and selection are among the most common problems of statistical practice. Some of the most commonly used method for model selection are; Akaike Information Criterio (AIC), Deviance Information criteria (DIC), and Bayesian information criteria (BIC). In this study, the AIC criteria, BIC criteria and i-likelihood areused to compare various candidates of shared semi-parametric frailty models. The model with the smallest AIC value is considered a better fit.*AIC* providing a balance between models fit (via the log-likelihood) and model effective degree of freedom [46, 68]advocated that, givena class of competing models for a data set,one choose the model that minimizes:

$$AIC = D(\hat{\theta}) + 2P \qquad 3.28$$

Where, p represents the number of parameters of the model. $D(\hat{\theta})$ Represents an estimate of the deviance evaluated at the posterior mean, $\hat{\theta} = E(\theta / data)$ .The deviance is defined by, $D(\theta) = -2\log L(\theta)$ where θ is a vector of unknown parameters of the model and $L(\theta)$ is the likelihood function of the model.

The AIC penalizes the number of parameters less strongly than the Bayesian information criterion (BIC) [68, 69]. The AIC tends to overestimatethe number of parameters needed, even asymptotically [69].Hence, BIC are used instead of AIC and it's formula is;

$$BIC = D(\hat{\theta}) + p\log n \qquad 3.29$$

The most benefit of the BIC approximation is that it includes theBIC penalty for the number of parameters being estimated. The modelwith the smallest BIC value is chosen as the best model

CHAPTER FOUR

4 Result and Discussion

4.1 Descriptive Statistics

The descriptive statistics of the study showed that about 3580 (84.39%) percent of children were breast-fed (uncensored) and 662 (15%) not breast-fed (censored) according toEDHS2016 data set of this study in Ethiopia. Mothers from Tigray and Amhara regions prolongedduration of breast-fed;422 (92.34%) and 358 (92.26%) respectively relatively with median of survival time of 12 months which weresimilar.Oromia and Gambella regions were experienced nearly similar weaning times which were 550 (85.53%) and 238 (85.92%) with medians of survival time12 and 13 months respectively. Dire Dawa and Harari regions again experienced very similar weaning times which were 182 (82.35%) and 205 (82.32%) withmedians of survival times 12 months and 13 months from birth respectively. Children from Somali region experienced the least breast-fed duration which was 405 (71.93%) with 11 month median of weaning time. The secondand third regions with least duration of breast-fed wereAffarand Addis Ababa which were about310 (79.08%) and172 (80.37%)with medians survival duration of 12 monthsweaning which were similar. The region with the third highest duration of breast-fed was Benshangul which was about301 (90.09%)with 12 month survival median on breast-fed.

Mother's with age group 15-19 and 20-24 were experienced very close duration of breast-fed 236 (82.51%) and 865 (82.93%) respectively which were the least in the groups. Their medians of weaning time were 9 months and 11 months respectively. Mothers' from Christians religions were experienced more breast-feeding practice which were 1113 (89.14%) and 740 (88.37%) from orthodox and protestant religion followers respectively with similar medians of 12 months of weaning time. Children from Ethiopian rural areas relatively enjoyed more breast-fed duration than those from the urban areas which were 2871 (84.99%) and 864 (82.06%) respectively with medians of 12 months weaning time. Mothers' with primary school experienced more breast feeding 1032 (87.65%) than others with weaning median time of 11 months and mothers with higher education experienced less breast-fed duration 141 (77.05%) with medians time of breast-feeding 13 months. More numbers Ethiopian motherscategorized as the poorest class according to Rural/Urban combined wealth index of EDHS 2016 report. Accordingly about 1234 (82.65 %)

of this class of mothers spent breast-fed with 12 months medians of weaning time. The mothers with the middle income spent better time on breast-fed which was about 516 (87.90%) with 12 months medians. From mothers currently using contraceptive methods about 950 (88.53%) were breast-fedwith medians of weaning time 14 months and it seemed better than those who were never used and used since birth. Mothers who were used contraceptive before last birth were possessed higher percentage of breast-fed in this category 617 (89.68%) with 12 months medians survival of weaning time.There was very small discrepancy on gender of infants which were 1770 (83.965%) and 1810 (84.81%) for males/females infants/babies respectively with both 11 months medians of weaning time. There were some gab between mothers visited by health worker in past 12 months and those did not visited by health worker which were 1190 (88.8%) and 2390 (82.35%) respectively with medians of weaning time 12 months for mothers visited by health worker in the past 12 months and 11 months for those didn't visited by health worker.

Table 2: Descriptive summary for mothers breast-fed duration by categories of covariates. N=number children at risk, CI= confidence interval, HW=health worker

Covariates names	Variable categories	N at risk	Events	Weaning Medians	95% CI
Regions	Tigray	457	422(92.34%)	12	(10 13)
	Affar	392	310(79.08%)	12	(10 13)
	Amhara	388	358(92.26%)	12	(10 13)
	Oromia	643	550(85.53%)	12	(11 13)
	Somalia	563	405(71.93%)	11	(10 12)
	Benshangul	331	301(90.09%)	12	(11 13)
	SNNPR	507	437 (86.19%)	12	(11 13)
	Gambela	277	238 (85.92%)	13	(11 14)
	Harari	249	205 (82.32%)	12	(11 13)
	Addis Ababa	214	172 (80.37%)	12	(11 14)
	Dire Dawa	221	182 (82.35%)	13	(11 15)
Mothers' Age group	15-19	286	236 (82.51%)	9	(7 11)
	20-24	1043	865 (82.93%)	11	(10 12)

	25-29	1220	1030 (84.42%)	12	(11 12)
	30-34	897	767 (85.50%)	12	(11 13)
	35-39	572	494 (83.44%)	12	(11 13)
	40-44	180	151 (83.88%)	14	(12 16)
	45-49	44	37 (84.09%)	16	(14 18)
Religion	Orthodox	1271	1133 (89.14%)	12	(12 13)
	Catholic	27	23 (85.18%)	14	(11 20)
	Protestant	740	654 (88.37%)	12	(11 13)
	Muslim	2131	1701 (79.82%)	12	(11 12)
	Traditional	39	34 (87.17%)	14	(12 19)
	Others	34	29 (85.29%)	10.5	(7 20)
Mothers residence	Urban	864	709 (82.06%)	12	(11 13)
	Rural	3378	2871(84.99%)	12	(11 12)
Education level	No education	2516	2101 (83.50%)	12	(12 12)
	Primary	1176	1032 (87.75%)	11	(10 12)
	Secondary	365	306 (83.83%)	11	(10 13)
	Higher	183	141 (77.05%)	13	(11 15)
Combined wealth index	Poorest	1493	1234 (82.65%)	12	(11 12)
	Poorer	710	601 (84.64%)	12	(11 12)
	Middle	587	516 (87.90%)	12	(11 13)
	Richer	535	464 (86.72%)	12	(11 13)
	Richest	917	765 (83.42%)	12	(11 13)
contraceptive use	Currently using	1073	950 (88.53%)	16	(1315)
	since last birth	104	70 (67.31%)	15	(1620)
	Before last birth	688	617 (89.68%)	12	(7 9)
	Never used	2377	1943(81.74%)	12	(11 12)
Currently working	No	3174	2684 (84.56%)	11	(11 12)
	Yes	1068	896 (83.89%)	13	(13 14)
Children gender	Male	2108	1770 (83.96%)	12	(11 12)
	Female	2134	1810 (84.81%)	12	(11 12)
Antenatal care visit	No	2754	2383(86.53%)	11	(11 12)

	Yes	1327	1067(80.41%)	12	(12	12)
Visited by health worker	No	2902	2390 (82.35%)	12	(12	12)
	Yes	1340	1190 (88.80%)	11	(1012)	
Husband educational status	No education	1837	1537(83.67%)	12	(12	12)
	Primary	1346	1181(87.74%)	11	(11	12)
	Secondary	463	378(83.58%)	11	(11	13)
	Higher	358	301(84.07%)	10	(10	13)
	Don't know	32	28(87.5%)	9	(6	16)

Mothers whom husbands get primary educational status better spend on breast-fed of their children i.e. 1181(87.74%) relative to others with 11 months median of weaning time. Mother who didn't know their husband educational status possessed the second longer time of breast-fed 28 (87.5). The mothers with husbands who achieved secondary educational levels, higher and no education possessed very close duration of breast-fed with 11, 10, and 12, medians of weaning time respectively.

4.2 The Kaplan-Meier (KM) Survival Curve for Different Groups

The resulting KM survival curve based on EDHS 2016 children weaning time data set were shown in the following figures. Note that in these plots survival time isbeing measured in months; thus the probability of survival of time to wean was plotted against time. From figure 4.1 below there were no clearly significant difference visible in terms of duration of breast based on religion covariate categories. Mothers from Catholic religion followers'had low breast-fed duration at beginning and lower at the middle relative to other religions followers relatively. Mothers' from Muslim and orthodox religion in Ethiopia spent more duration of breast-fed according to Kaplan-Meier curve below compared to other religion followers mothers relatively. According to this variable i.e. religions categories there were children who weaned before six months age as it can be seen from figure 4.1 of survival weaning time probability less than unit at the beginning life of children.This showedthat the exclusive breast-fed practice in Ethiopia was less than the internationally recommended one.Thus, the survival probability of weaning time was expected to be one for the first six month of infants'ages.

From figure 4.2 below, it can be seen that there were no clear differences of time to wean in Ethiopian children in terms of mothers education status relatively.Mothers with higher education status relatively showed more survival probability of weaning time compared to other mothers' education levels relatively according to Kaplan-Meier curve of EDHS 2016 data set.

Figure 4.1 KM survival estimate for Mothers' religions.

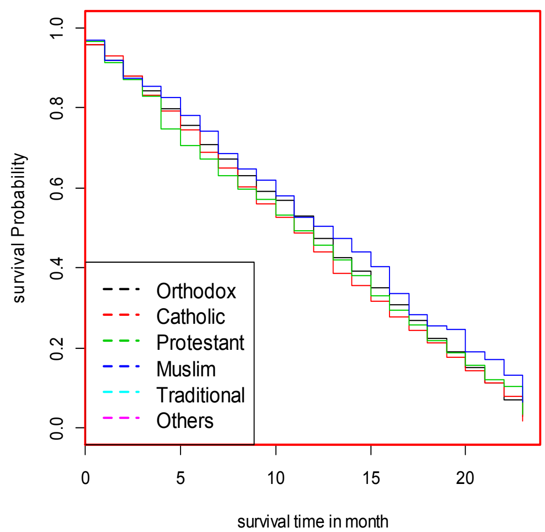


Figure 4.3 KM survival estimate for residences catagories

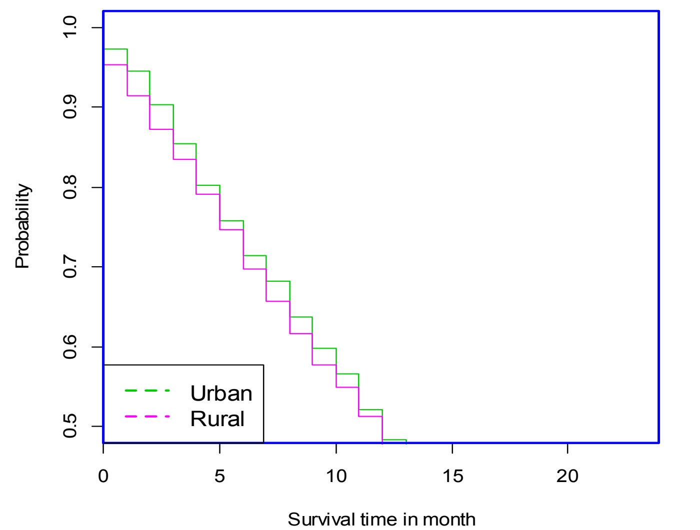


Figure 4.2 KM survival estimate for Mothers edu status.

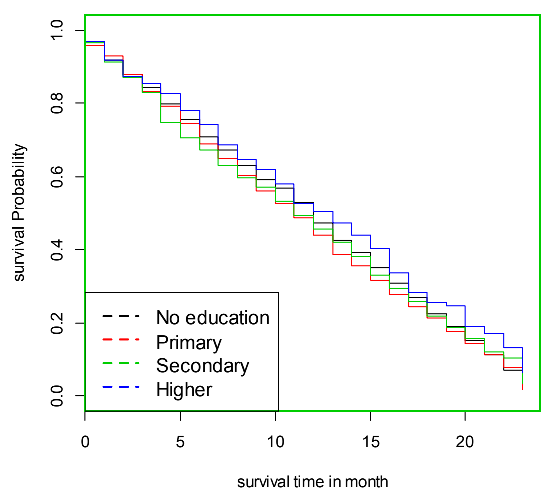
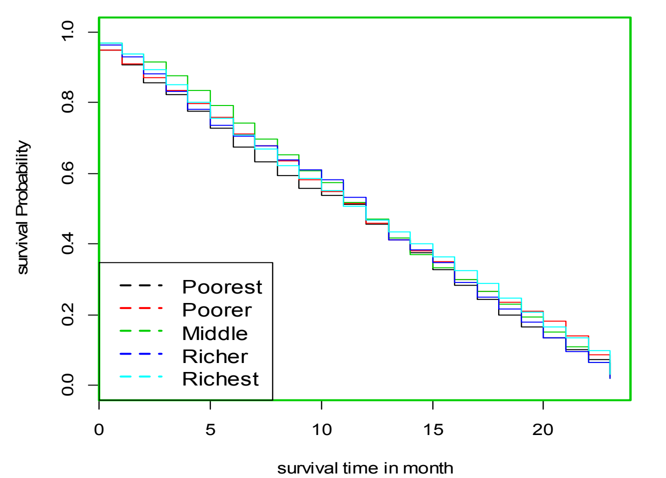


Figure 4.4 KM survival estimate for family wealth status.



Mothers with primary education level, no education and secondary showed relatively almost similar survival probability of breast-fed duration/ showed early weaning time comparatively. From figure 4.3 above; mothers who live in Urban Ethiopia had spent more time on breast-fed of their childrencompared to mothers live in rural areas all the time relatively.

Figure 4.5 KM survival estimate for Mothers agegroup.

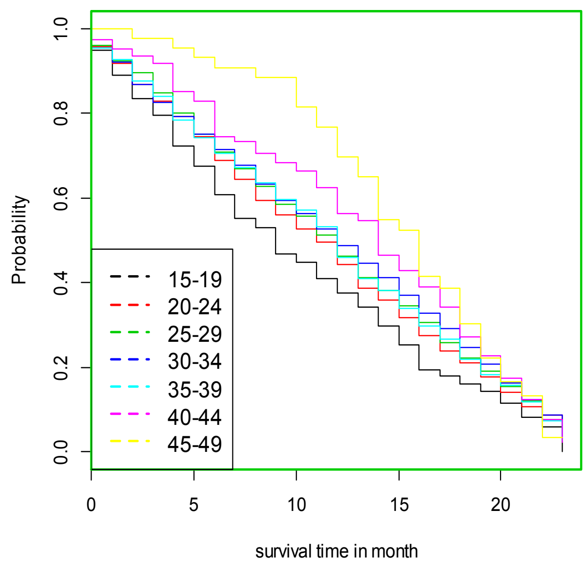


Figure 4.6 KM survival estimate for work status categori

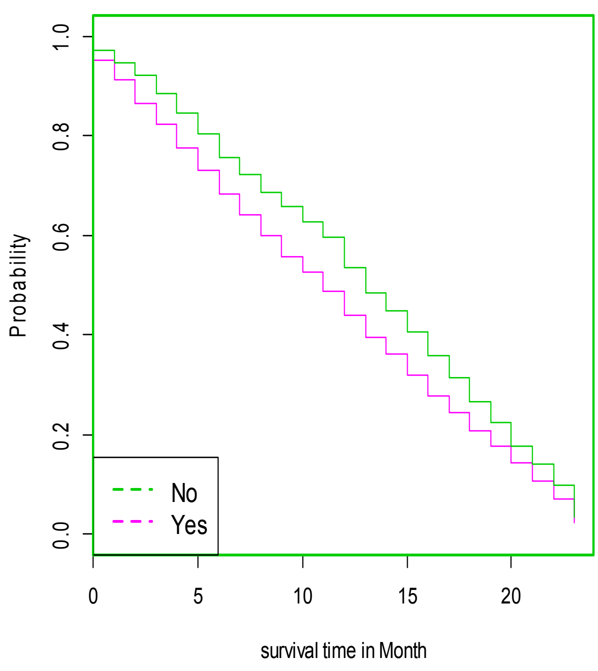


Figure 4.7 KM estimate for children gender categories.

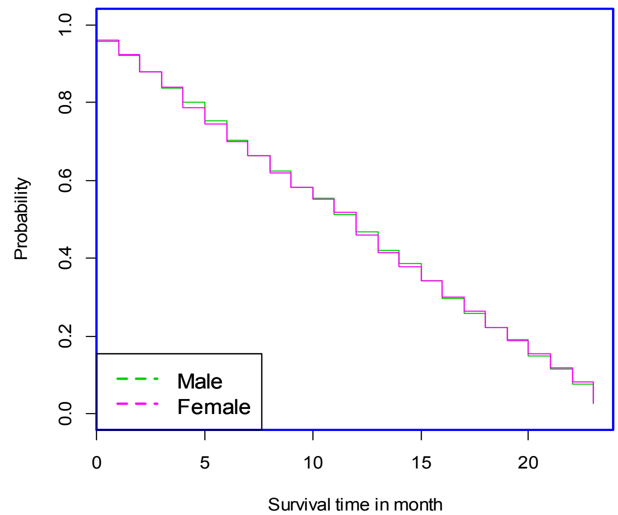


Figure 4.8 KM survival estimate for ANC visit catagories.

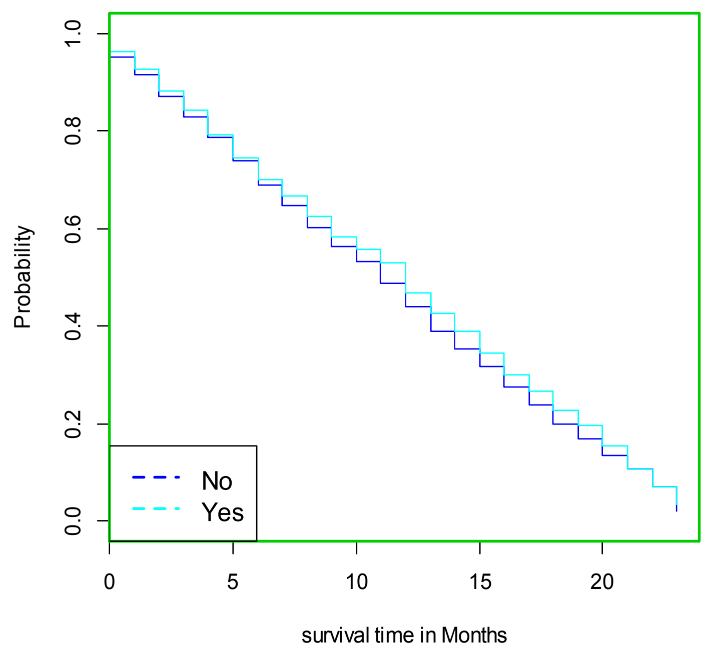


Figure 4.9 KM survival estimate for Mothers visited by HW

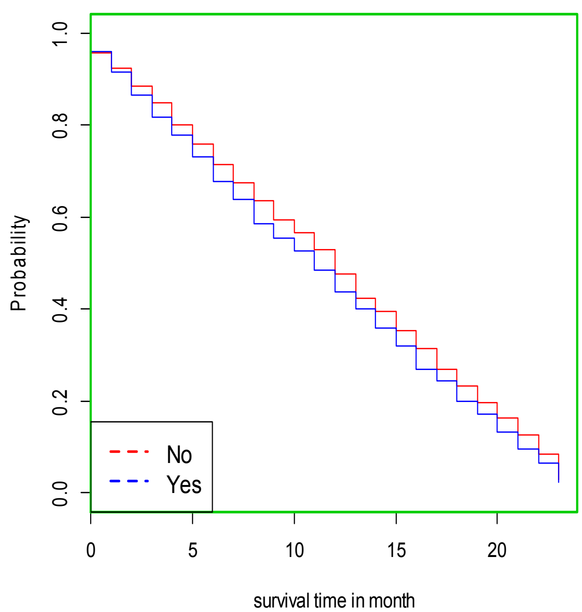


Figure 4.10 KM survival estimate for family planning use.

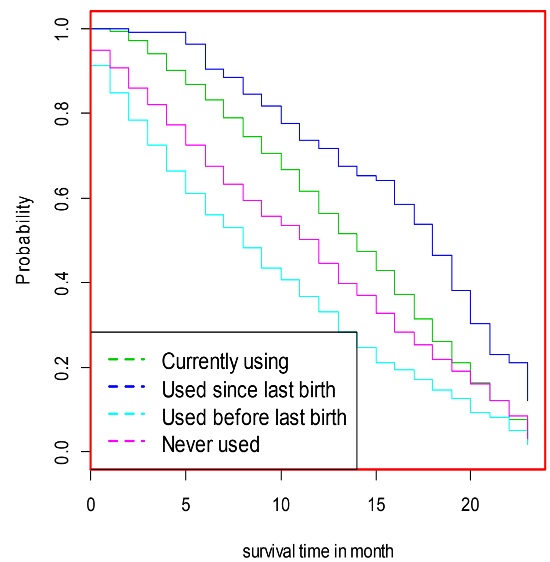


Figure 4.11 KM survival estimate for husband edu level.

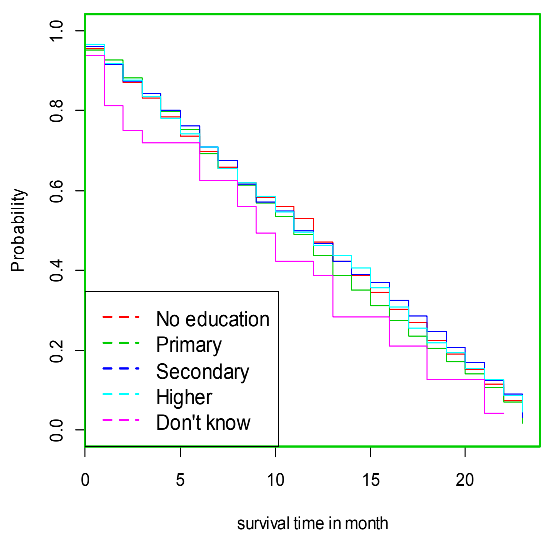
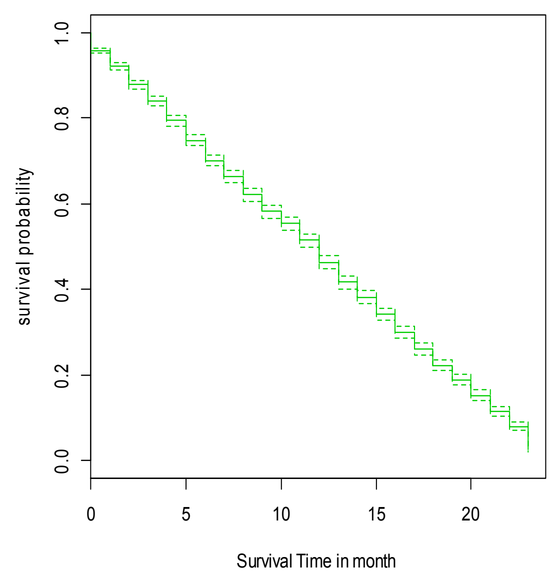


Figure 4.12 Overall Kaplan-Meier survival estimate



From figure4.4 above it can be seen that there were no clear cut deffirrences of breast-fed survival time/time to wean based on family wealth index. Mothers in the richest class showed better duration of breast-fed at first three months and middle ages(10-20) months of children age. Mothers in the class of middle showed relatively better time to wean most probably at 2-8 months of children age and mothers in the class of richer showed relatively shorter period of breast-fed.

From figure 4.5 above showed that there were very clear cut differences of survival probability of weaning time within maternal age group. Accordingly maternal age group of 45-49 spent more survival probability of weaning time/late weaning time compared to others maternal age groups relatively. Mothers in the age group 40-44 possessed the second highest survival probability of duration of breast-fed/the second late weaning time relatively. On the other hand maternal age group 15-19 spent less time of survival probability of duration of breast-fed/possessed very early weaning time compared to other maternal age groups relatively. Mothers in the age group of 20-24 showed the second least of early weaning of their children.

From figure 4.6 above mothers on working currently possessed longer survival probability of weaning time relatively compared to mothers not working. From figure 4.7 above there were not clear differences of survival probability of weaning with respect infants genders relatively. Thus female and male infants seemed to have same survival probability of weaning time. From figure 4.8 above mothers who visited antenatal care had higher survival probability of weaning time compared to those not relatively. Figure 4.10 above shows very clear difference of duration of breast-fed with regard to mothers' pattern of contraceptive use. Accordingly mothers in the groups of used since last birth and mothers' currently using were possessed the first and second highest survival probability of weaning time relatively. Mothers in the group used before last birth of contraceptive method and never used seemed the first and second least of survival probability of early weaning time respectively.

From figure 4.11 above mothers with husband educational status of don't know/the respondents didn't know their husband educational level seemed lowest survival probability of weaning time. The other categories of the groups possessed nearly similar survival probability of weaning time. Figure 4.9 above showed mothers visited by health worker in the last 12 months possessed less survival probability of weaning time/ weaned their children early. Figure 4.12 showed the overall survival probability of weaning time in Ethiopia. Accordingly there were huge gaps between WHO and UNICEF recommendation of duration of breast-fed and what duration of Ethiopian children breast-fed on in this study.

4.3Comparison of Survival Experience using log rank and Peto tests

Log-rank test and Peto tests were used for survival estimates to look the significance of the difference in survival experience of time to wean among different categories in this study. The results of the Log-rank and Peto tests for the equality of survivor functions were presented in as fellows.The Log-rank and Peto tests results showed that survival difference of weaning time with mothers' age groupwere statistically significant at alpha=0.05 level of significance as the p-value was small. With respect to mothers' current work status the difference of weaning time were statistically significant at alpha = 0.05 level of significance as its p-value was smaller. With regard to mothers residential; the difference of weaning time was statistically significant at alpha = 0.05 level of significance as it p-value was smaller. The log-rank test of difference with mothers' pattern of contraceptive use were statistically highly significantat alpha=0.05 level of significance as its p-value was smaller with regard tobreast-fed survival time.

Regarding regions and ANC visit different results were observed for both tests i.e. for log-rank test their insignificance of differences in breast-fed survival time and for peto test their significance of differences in breast-fed survival time at alpha=0.05 level of significance as its p-value was smaller. With regard of Mothers' education level there was no survival difference of weaning time statistically at alpha = 0.05 level of significance as its p-value was larger. There was also no difference of weaning time with regard to children gender statistically at alpha =0.05 level of significance as its p-value was larger. With mothers' religion there was no survival weaning difference statistically at alpha = 0.05 level of significance as its p-value was larger. When family wealth index was tested there no weaning difference statistically at alpha = 0.05 level of significance as its p-value was larger. With regard to husband education status there were no significant differences at alpha =0.05 level of significance in terms of breast-fed survival time as its p-value was larger.

Table 3: Comparison of Survival Experience of Ethiopian children weaning time Using Log-rank and Peto test (Ethiopian Demographic and Health Survey, 2016)

Covariates categories	*Degree of freedom*	*Log-rank test*		*Peto test*	
		Chi-square	*p--value*	*Chi-square*	*p-value*
Mothers age group	*6*	*35.2*	*4e-06*	*24.6*	*4e-04*
Region	*10*	*12.6*	*0.2*	*20.2*	*0.03*
Religion	*5*	*4.8*	*0.4*	*3.9*	*0.6*
Residence	*1*	*4.7*	*0.03*	*6.1*	*0.01*
Mothers Education level	*3*	*5.2*	*0.2*	*5.6*	*0.1*
Family wealth index	*4*	*6.5*	*0.2*	*5.8*	*0.2*
Current mothers work status	*1*	*36.8*	*1e-09*	*27.4*	*2e-07*
Children gender	*1*	*0*	*0.9*	*0*	*0.9*
Husband education status	*4*	*3.7*	*0.4*	*5.4*	*0.2*
HW visit in the last 12 months	*1*	*8.3*	*0.004*	*8.9*	*0.003*
Pattern of contraceptive use	*3*	*201*	*<2e-16*	*125*	*<2e-16*
Antenatal care visit	*1*	*3.4*	*0.06*	*3.8*	*0.0*

4.4 Evaluation of the Cox Proportional Hazard Assumptions

It is crucial point to show the violation of cox regression model for the progression of the next model for amendment. Thus, the proportional hazards (PH) assumption can be checked using statistical tests and graphical diagnostics based on the *scaled Schoenfeld*residuals. From the annex table A, it could be observed that the global test of the proportional hazard assumption were rigorously violated at alpha=0.05 level of significance as the global p-value was too small.

Those covariates violating the PH assumption were few parts of mothers' age group, few parts of patterns of contraceptive use, mothers' work status and few parts of mothers' educational status as it can be seen from annex table A1. This shows good evidence to extend the cox regression model to the cox stratified model and shared frailty models too, or accelerated failure time model, hence in this thesis cox stratified model and semi-parametric shared frailty model were used.

4.5. UnivariableFrailty Model Analysis

All the covariates in the study were considered for univariable frailty model analysis. Accordingly from appendix A3, the maternal age group categories were statistically significant predictive factors for early time to wean at alpha=0.05 level of significance as their p-value were small compared to alpha=0.05. Mothers residential area, mothers' work status, mothers' visited by health worker in last 12 months were another statistically significant predictive factors for early weaning time at alpha =0.05 level of significance as their p-value were small compared to alpha value=0.05 which can be seen from appendixof table A3.

Mothers' husband education level, mothers' religion, children gender and family wealth index were not statistically significant predictive factors at alpha=0.05 level of significance for early weaning time in Ethiopia using univariable frailty modelas it can be seen from appendix of table A3.Therefore, based on this result, it is better to ignore the children gender, husband education level, mothers religion and family wealth index covariates and shall do our multivariable analysis using all the left significant factors.

4.5 Multivariable Analysis and Model Comparisons

The multivariable survival analysis in this study was performed using the covariates; mothers' residence, work status of the mothers, mothers' educational status, patter of current contraceptiveuse of the mothers, mothers visited by health worker in the past 12 monthsand mothers' antenatal care visit. In this study, author used;i-likelihood ratio value, AIC criteria and BIC Criteriato compare various candidates of semi-parametric shared frailty models. The model with the smallest AIC value, likelihood value and BIC criteria is a model which better fit the given data.The table below presented region-specific model (gamma frailty, lognormal frailty or

Gaussian and t frailty models) results for regional endpoint. It can be seen that there were no clear difference between Gammas shared frailty model and log-normal shared frailty model based on AIC and i-likelihood values.Thus, the author based on BIC value for model selection.Accordingly gamma shared frailty model seemed the best model as its BIC value was too small and used in this thesis for covariate determination.

Table 2; AIC value, BIC and i-likelihood for multivariable semi-parametric shared frailty models EDHS 2016.

Multivariate model types	AIC	BIC	I-likelihood
Shared Gamma	51108.95	51232.18	-25534.43
Shared lognormal	51108.6	51237.52	-25533.32
Shared Gaussian	51108.42	51238.23	-25539.66
Shared.t	51113.18	51277.98	-25529.78

Using multivariable semi-parametric gamma shared frailty model; the covariate of all mothers' age group was statistically significant predictive factors as its 95% confidence interval (CI) didn't include one(1) for early weaning time in Ethiopia according to EDHS 2016 data set output. This indicates that it is the most important covariate factor for the time to early weanof Ethiopian children.Similarly pattern of mothers'contraceptive use was statistically significant predictive factors as its' 95% confidence interval didn't include one (1) for early weaning time in Ethiopia.

Mothers' working status was also statistically significant predictive factors for early time to wean in Ethiopia as its 95% confidence interval (0.7665 0.8997) didn't include one (1). Mothers visit ANC was statistically significant predictive factors as its 95% confidence interval(0.8337 0.9797) didn't include one (1) for early time to wean in Ethiopia. Lastly mothers visited by health worker in the last 12 months was also statistically significant predictive factor as its 95% confidence interval (1.0406 1.2050) didn't include one (1) for early time to wean in Ethiopia. All mothers' education level categories were not statistically significant factor for time to early wean in Ethiopia as its 95% confidence interval include one. Mothers' residential though statistically significant when univariable frailty model applied the finding were not supported in multivariable shared frailty model i.e. (0.9223 1.1355). The same conclusion was reached when alpha 0.05 level of significance are considered i.e. mothers' age group, mothers visited by health worker in the last twelve months, mothers' work status, pattern of mothers contraceptive use and mothers visited prenatal care were statistically significant factors for early weaning time as their p-value were small compared to alpha value according EDHS of 2016 children data set. On the other hand mothers' education level and mothers' residence were not statistically significant predictive factor for time to early wean in Ethiopia at alpha=0.05 level of significance.

Table 5 Multivariable analysis using the gamma shared frailty model, EDHS 2016

Parameter	Coefficients	Hazard ratio	SE	95% CI		p-value
Mothers' age group						
15-19(ref)						
20-24	-0.20069	0.8182	0.07465	(0.7068	0.9471)	7.2e-03
25-29	-0.26892	0.7642	0.07443	(0.6605	0.8842)	3.0e-04
30-34	0.32013	0.7261	0.07803	(0.6231	0.8460)	4.1e-05
35-39	-0.29647	0.7434	0.08281	(0.6321	0.8744)	3.4e-04
40-44	-0.47709	0.6206	0.10751	(0.5027	0.7662)	9.1e-06
45-49	-0.64000	0.5273	0.17914	(0.3712	0.7491)	3.5e-04
Residence						
Urban(ref)						
Rural	0.02310	1.0234	0.05304	(0.9223	1.1355)	6.6e-01
Educational status						
No education(ref)						
Primary	0.03555	1.0362	0.04338	(0.9517	1.1281)	4.1e-01
Secondary	0.07040	1.0729	0.07134	(0.9329	1.2340)	3.2e-01
Higher	0.05745	1.0591	0.10017	(0.8703	1.2889)	5.7e-01
Visited by HW						
No(ref)						
Yes	0.11314	1.1198	0.03741	(1.0406	1.2050)	2.5e-03

Contraceptive use						
Currently using(ref)						
Since last birth						
Before last birth	-0.48472	0.6159	0.12425	(0.4828	0.7857)	9.6e-05
Never used	0.54635	1.7269	0.05400	(1.5535	1.9198)	4.6e-24
	0.25386	1.2890	0.04511	(1.1799	1.4082)	1.8e-08
Work status						
No (ref)						
Yes	-0.18579	0.8304	0.04087	(0.7665	0.8997)	5.5e-06
ANC visit						
No(ref)						
Yes	-0.10121	0.9037	0.04118	(0.8337	0.9797)	1.4e-02

4.6 Assessing the Heterogeneity Parameter among Regions

From anova test of homogeneity, the random effects estimates for all the regions were significantly different from zero (0). In addition, a formal test for the need of regions random effect was conducted by comparing the partial log-likelihood for the models with and without the frailty term. For the gamma frailty, the change in the partial log-likelihood was;

-2(25534-25541) =14 ; $\chi^2_{0,1}$=12.605 ,based on this result the null hypotheses were rejected as chi-square calculated is greater than tabulated chi-square and concluded that the random effect(the variation of time to early wean across the region) is highly significant and the model that account those variation are recommended.

In addition the resulting P-value0.01392 was also supports evidence to reject the null hypothesis ofhomogeneity between the regions. Similarly, for the lognormal frailty model, thechange in partial log-likelihood with inclusion of the frailty was;

$-2(-25541+25533)=16$; $\chi^2_{0;1}$=14.808 , based on this result the null hypotheses were rejected as chi-square calculated is greater than tabulated chi-square and concluded that the random effect(the variation of time to early wean across the region) is highly significant and the model that account those variation are again recommended.In addition the resulting P-value0.01102was also supports evidence to reject the null hypothesis of homogeneity between the regions.

The random effect (θ) was highest when we assume the Gaussian frailty distribution (θ= 00363) and the smaller with gamma frailty distribution (θ=0.002532) for unspecified baseline hazard distribution. The Kendall's tau (τ) was highest for the highest θ values. Accordingly the dependency within the clusters for the Gaussian shared frailty model (τ=0.00181) was the maximum and minimum for gamma shared frailty model (τ=*.001264)*.

4.6 Cox Stratified and Shared Frailty models Comparison

The similarity between the cox stratified model and shared frailty models could be further attributed to the fact that for the frailty models, the heterogeneity parameters were very small or the researcher may not interested on variation across the subject under study. From the above section it realized that there were significant variations of weaning time across the region and shared frailty model were recommended over cox stratified model to account the variation across the regions. The hazardratio for shared lognormal and shared gamma frailty models were small compared to the cox stratified model. The SE for cox stratified model was large compared to the shared frailty model in this study showing that shared frailty model for this data type were advisable as it can be seen from appendix table A6. Similar determinant factors for early weaning time were reached using both models (shared frailty versus cox stratified) except one covariate; which was significant when shared frailty model applied and not when cox stratified model was applied as it can be seen from appendix table A4.

4.7 Discussion

The median of time to wean in Ethiopian according to EDHS 2016 children data set in this study is 12 months. Another study by MelkamuMolla and LeakemariamBerhe showed that the median of actual weaning time in Ethiopia was 24 months [11].The result of this study suggested that age group of the mothers were statistically highly significant predictive factors for time to wean of Ethiopian children. This shows that mothers who are in the age group of 15-19 and 44-49 were the highest and the least survived on the time to wean respectively compared to other age groups. This might be due in maturity to hold the responsibility of leading the house for mothers in the age group 15-19 and their married situation might not base on their interest.

On the other hand mothers in the age group 44-49 in Ethiopia were the real age of exercising strong leadership of the household with high maturity and that why they were the highest survived of the weaning time for their children. Mothers in the age group 35-39 and 40-44 were the third and second survived of weaning time in Ethiopia respectively. They possessed nearly similarly survival of weaning time. Mothers in the age group 20-24 were the second least of survived time of weaning according to EDHS 2016 data set. Another study conducted in Ethiopia by MelkamuMolla andLeakemariamBerhe found mothers age group were the most significant predictive factors for time to wean[11]. Another study in Iran conducted by Gholamrezaet.al (2011) found that maternal age were the significant predictive factors for time to wean in north Iran. This might be due the awareness provided while they received treatment from health professional at the health facilities.

Many other studies have also demonstrated that maternal age at the time of birth influenced breastfeeding initiation and duration [38]. The results of this study suggest that work status of the women had a significant effect on infants weaning time and weaning time was higher for women who were on work status. Women who are employed are less likely to quit breastfeedingearly when compared with women working as administratorsand in manual jobs [70, 71].Though, Women's work may have a negative impact on breastfeeding because of inadequate time to breastfeed they have spent more duration of their children breast-fed relatively[70]. Similar study by AbebawWasie et.al (2017), reached Antenatal care was another important predictive factor for weaning early weaning time in Ethiopia[58].

From this study result 95% confidence interval for antenatal care was [0.8104 0.9591]for gamma shared modelwhich did not include one and witnessed for the above evidence.Mothers who did not attend antenatal clinic during pregnancy may have apoor initiation and exclusivity of breastfeeding[72]. Study by Wilhelm, Rodeherst, was also another witnessed for this study achievement [73]. Antenatal attendance is a potential determinant of infant feeding practice[40]–42]. The study conducted in Zimbabwe by MunjomaTakudzwa Pamelarevealed that infant gender was not the predictive factor for the weaning timeof Zimbabweans infants[74]. This study also supported the study of MunjomaTakudzwa Pamela as the confidence interval for gender factors include one according to EDHS 2016 data set.Clinicians and health workers may have an influential role in breastfeeding initiation and continuation [74].

From the result of this study health worker visit was another significant predictive factors for weaning time in all model used. Another study by Ahmed identified support for mothers immediately after delivery as a way of overcoming breastfeeding problems and enhancing confidence[41].From the result of this study maternal educational status and husband educational status were not significant predictive factor for weaning time according to EDHS 2016 children. But another study in Ethiopia by MelkamuMolla and leakemariam revealed that maternal educational status of higher was significant predictive factors for early weaning time of infants [11]. The discrepancy between this study finding and study by MelkamuMolla and LeakemariamBerhe might be due coverage of media and accessibility of health in fractures in all parts of the country region today. Study in north Iran revealed that maternal educational status was not significant predictive factor of weaning time [39].

According to study in northern Iran the father's educational status and economic status did not have any correlation with either EBFD or BFD[43]. In this study we found household combined wealth index was not significant predictive factor for survival weaning time of Ethiopian infants. Another study in Ethiopia conducted by MelkamuMollaand LeakemariamBerhe supports the finding. From this study all three models used revealed that mothers religion were not significant predictive factor for the survival of weaning time of Ethiopian infants. That's the 95% confidence interval for this factor didn't include one in all three factors and the p-value for cox stratified regression was less than alpha 0.05. But study by MelkamuMolla and LeakemariamBerhe contradicts the finding [11]. This discrepancy may be due to long distance time of data used. The pattern of contraceptive use was another important predictive factor for weaning time of Ethiopian infants. Another study in Ethiopia by MelkamuMolla and LeakemariamBerhe revealed very similar finding using different term for[11].

CHAPTER FIVE

5. Conclusion and Recommendation

5.1 Conclusion

From the study comparison of various semi-parametric shared frailty models for the Ethiopian children was performed using the AIC criteria, i-likelihood-value and BIC criteria, where a model with minimum AIC, i-likelihood and BIC criteria value is accepted to be the best. Accordingly, gamma shared frailty model was with thealmost similar value of AIC, i-likelihood and smallest BIC values, thus it was considered as the best model for under two year weaning time of Ethiopian children. Another case was for cox stratified model where all values i.e. AIC criteria, BIC criteria and i-likelihood was incomparable to gamma shared frailty modeland lognormal shared frailty model in this study. Thus it needed to assess the validity of the regional variation/random effect (θ) as this thesis interested in the variation of random effect (θ) too.Based on statistical actual test of heterogeneity among the regions of Ethiopia i.e. chi-square calculated = 16 and tabulated chi-square at 0 and 1 degree of freedom = 14.808; showed that the variations of early time to wean across the regions were statistically significant. The random effect for both semi-parametric gamma frailty distribution and lognormal frailty distribution were highly significant in this study indicating that there are variation of weaning time across Ethiopian regions.

The Schoenfeld test showed that the assumption of marginal cox regression model was statically insignificant as its global p-value was very small compared to alpha value i.e. p-value=0.000< alpha=0.05. Hence, both semi-parametric shared frailty and cox stratified were used as the assumption of ordinary cox regression was rigorously violated based on actual proportional hazard test.The model comparison in semi-parametric frailty distribution is not as simple as the case of the parametric frailty distribution due to the base line hazard distribution function is unspecified. In this study very close result was reached using both semi-parametric shared frailty model and cox stratified model regarding determination of early weaning time factors.The stratified regression possessed large hazard ratio (HR) values compared to the semi-parametric shared frailty model. The SE for gamma and log-normal shared frailty model were smaller compared to cox stratified model output as it can be seen in the appendixes of table A6. That indicates shared frailty model were more appropriate for the weaning time data set of EDHS 2016.

The determinant factors considered were maternal age group, residence of women, educational level of women,religion of women, work status of women, mothers antenatal care visit, wealth index of household,head educational level, mothers visited by health work in the last 12 months and pattern of contraceptive use.Analysis using gamma shared frailty model showed that maternal age, mothers working status, mothers visited bay health work, pattern of contraceptive use, andmothers attended antenatal care were statistically the most significant factorsfor the time to early wean of Ethiopian children due to their 95% confidence interval were not include one (1). Similar conclusion was reached when alpha α=0.05level of significance considered astheir p-value were smaller compared to alpha value for all covariates. When cox stratified model used similar determinant factors for early weaning time were reached for almost all covariates as it can be seen from appendix table A3.

From the log-rank and peto tests of annex table A1there were statistically significant difference of early time wean among maternal age group, current work status of mothers, mothers visited by health worker in the last 12 months, mothers residential area, mothers who visit antenatal care and contraceptive use. Accordingly mothers in age group 44-49 had prolonged weaning time followed by age group 40-44 and 35-39 respectively. Mothers in the age group 15-19 and 20-24 spent the least weaning time respectively. Concerning pattern of contraceptive use, mothers used contraceptive method since last birth, had prolonged weaning time of their children followed by mothers currently using compared to mothers not using the method. Similarly mothers visited by health worker in the last twelve month had better weaning time than mothers didn't get that chance. Mothers working currently had prolonged their infants' breast-fed duration according to this study than those not working.

This study also revealed that, of all 4242 mothers owned infants under twenty four(24) months old aged 15-49, 3580 (84.39%) were breast-fed and the median for Ethiopian under two year children breast-fed were 12 months. The median survival of weaning time in Ethiopia was not equal in most regions. It is lowest for somalia regions, while highest for Gembela and Diredawa administration city when compared to other regions. This study again revealed that the survival probability of weaning time in Ethiopia was about (70%) when the children age of six monthconsidered. Similarly when children in Ethiopia at age 12 months considered the survival probability of breast-fed was 46% which less than half and 2.7% at the age of 23 months.

5.2 Recommendation

Based on the result of this study huge workswere waiting for, to make all the society responsible on awaking mothers to extend the duration of their infants breast-fed. WHO and UNICEF recommended infants to exclusive breast-fed for six months, but according EHDS 2016 data set of this study report about 15.61% of Ethiopian mothers weaned their infants before six months age even not exclusive breast-fed.When we came to the probability survival of early weaning time at the infants' age of six and twelve months in Ethiopia it was about 70% and less than 50% respectively. These had very huge side effects on children health up to their adulthood.

Maternal age was another determinant of the early weaning time in Ethiopia and we strongly recommend the ordinance of the legal age of marriage to be considered and take special attention for, especially infants of mothers in age range of 15-19 were in the high risk of early weaning compared to others age group in Ethiopia. The Ethiopian minister of social affairs and Ethiopian minister of Women and children affairs had better to give special attention for age at marriage for females jointly. Another recommendation that emerge from the study is that as it is crucial to improving mothers to extend birth intervals/ use family planning as pattern of contraceptive use was another highly predictive significant factor for early weaning time in Ethiopia.

The early weaning variations were observed in this study across the regions and independent study was recommended in each region for further discovery of determinant factors. That additional study was also important to identify the source of variations across the regions.

The mothers who met health worker in the last 12 months and visited ANC had better duration of breast and this relations have to be encouraged.Thus, it is recommended government health office and all concerned stakeholders had to be worked hard on it to improve more.

Regarding model; shared semi-parametric frailty models were more appropriate for weaning data set in Ethiopia as the weaning variation across the regions were highly significant. In addition the standard error for shared semi-parametric frailty models were small compared to cox stratified model.

References

[1] I. Seidu and R. Stade, “EXCLUSIVE BREASTFEEDING AND FAMILY INFLUENCES IN RURAL GHANA : A QUALITATIVE STUDY Supervisor :,” no. May, 2013.

[2] M. . Labbok, “Effects of breastfeeding on the mother. Pediatric Clinics of North America,” *1*, vol. 48, p. 143–158., 2001.

[3] M. Labbok, “Trends in exclusive breastfeeding: findings from the 1990s.,” *Hum. Lact.*, vol. 3, p. 22, 2006.

[4] H. L., “www.unicef.org.uk. .,” 2011. .

[5] L. Haddad, “www.unicef.org.uk,” 2011. .

[6] S. Ip, M. Chung, G. Raman, T. A. Trikalinos, and J. Lau, “A summary of the Agency for Healthcare Research and Quality’s evidence report on breastfeeding in developed countries.,” *Breastfeed. Med.*, vol. 4 Suppl 1, pp. S17-30, Oct. 2009.

[7] Central Statistical Agency [Ethiopia] and ICF International, *FEDERAL DEMOCRATIC REPUBLIC OF ETHIOPIA ETHIOPIA Demographic and Health Survey 2016 Key Indicators Report*. 2016.

[8] D. Diez, “Survival Analysis in R,” pp. 1–16.

[9] A. C. Of, V. Parametric, and F. Models, “By : Akalu Banbeta A Thesis Submitted to the Department of Statistics , College of Natural Science , Jimma University as a Partial Fulfillment for the Requirements of Master of Science (MSc) Degree in Biostatistics,” 2012.

[10] R. D. C. Team., “R: A language and environment for statistical computing. R Foundation for Statistical Computing: Vienna, Austria.,” 2008.

[11] L. MelkemuMolla, “Survival Analysis of Duration of Breastfeeding and Associated Factors of Early Cessation of Breastfeeding in Ethiopia.,” 2016.

[12] EtagegnehuAssefa3 Laykewold Elyas, 1 Amha Mekasha, 1 Amha Admasie, “Exclusive

Breastfeeding Practice and Associated Factors among Mothers Attending Private Pediatric and Child Clinics, Addis Ababa, Ethiopia: A Cross-Sectional Study," *Int. J. Pediatr.*, vol. Article ID, p. 9, 2017.

[13] David Collett, "Modelling Survival Data in Medical Research." pp. 1–390, 203AD.

[14] D. F. Analysis TS, "The Statistical Analysis of Failure Time Data Second Edition."

[15] D. G. Clayton, *(A model for association in bivariate life tables and its application in epidemiological studies of family tendency in chronic disease incidence. Biometrika 65, 141-151.* 1993.

[16] C. W. McGilchrist, C. A. and Aisbett, *Regression with Frailty in Survival Analysis. Biometrics 47.* 1991.

[17] S. Romdhane, "Frailty Modeling for clustered survival data : a simulation study," pp 1–22.

[18] J. Homola, "PS555 – Longitudinal and Event History Models Frailty Models," 2017.

[19] P. Duchateau, L. and Janssen, *Understanding heterogeneity in generalized mixed and frailty models*. 2005.

[20] O. J. SJ., *Proportional hazards models with frailties and random effects. Stat Med.* 2002.

[21] F. Vonta, *The frailty model*, vol. 36. 2009.

[22] J. Ripatti, S. and Palmgren, *Estimation of multivariate frailty models using penalized partial likelihood. Biometrics 56,*. 2000.

[23] R. D. C. Team, "R: A language and environment for statistical computing. R Foundation for Statistical Computing: Vienna, Austria.," 2008.

[24] L. Yes, L. Yes, and A. T. Therneau, "Package 'coxme,'" pp. 1–16, 2013.

[25] "Breastfeeding AA of PS on. Breastfeeding and the use of human milk. Pediatrics [Internet]. 2012 Mar [cited 2018 Apr 23];129(3):e827-41. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22371471." .

[26] Jemie, “www.iamnotthebabysitter.com/breastfeeding-in-ethiopia,” *iamnotthebabysitter*, 2013.

[27] 1 Amha Admasie 2 and EtagegnehuAssefa3. Laykewold Elyas, 1 Amha Mekasha, “Exclusive Breastfeeding Practice and Associated Factors among Mothers Attending Private Pediatric and Child Clinics, Addis Ababa, Ethiopia: A Cross-Sectional Study. Int J Pediatr.,” 2017.

[28] D. J. Matji, “WHO.Ethiopia Observes World Breast Feeding Week.Addis Ababa.”

[29] H. K. Y. Berhane, D. Haile Mariam, “Food and Nutrition,” in The Epidemiology and Ecology of Health and Diseases in Ethiopia, J. Haider, H. Kloos, and D. Haile Mariam, Eds., Shama Books, Addis Ababa, Ethiopia.,” 2006.

[30] D. H. Tewodros Alemayehu, Jemal Haidar, “Determinants of exclusive breastfeeding practices in Ethiopia,” *Ethiop.J.Health Dev*, vol. 2009, pp. 12–18, 2009.

[31] M. S. Kramer and R. Kakuma, “Optimal duration of exclusive breastfeeding.,” *Cochrane database Syst. Rev.*, vol. 8, no. 8, p. CD003517, Aug. 2012.

[32] A. DG, “Suboptimal analysis using ‘optimal’ cutpoints.,” *Cancer*, vol. j78, pp. 556–557, 1998.

[33] S. M. (1997) Schmoor C, *Effects of covariate omission and categorization when analysing randomized trials with the Cox model. Stat Med*, vol. 16. 1997.

[34] S. T. Klein, J. P., Moeschberger, M. L., Li, Y. H. and Wang, “Estimating Random Effects in the Framingham Heart Study. In Survival Analysis.,” *State Art, J. P. Klein P. Goel, eds. Bost. Kluwer Acad. Publ.*, vol. 19, pp. 99–120, 1992.

[35] A. P. Ching-Ti Liu, PhD, *Biostatistics.Logistic Regression and Survival Analysis*. .

[36] H. P., *Analysis of Multivariate Survival Data, Springer-Verlag, Newyork*. 2000.

[37] S. Dhakal, T. H. Lee, and E. W. Nam, “Exclusive breastfeeding practice and its association among mothers of under 5 children in Kwango district, DR Congo,” *Int. J. Environ. Res. Public Health*, vol. 14, no. 5, 2017.

[38] A. R. Scott JA, Aitkin I, Binns CW, "Factors associated with the duration of breastfeeding amongst women in Perth, Australia.," *Acta Paediatr*, 1999.

[39] A. GholamrezaVeghari, AzadrezaMansourian, "Breastfeeding Status and Some Related Factors in Northern Iran.," vol. 26, 2011.

[40] A. H. Ahmed, "Breastfeeding preterm infants: an educational program to support mothers of preterm infants in Cairo, Egypt.Pediatric Nursing.," vol. 138, pp. 125–30, 2008.

[41] S. M. Agho, K.E., Dibley, M.J., Odiase, J.I. &Ogbonmwan, "Determinants of exclusive breastfeeding in Nigeria.BMC Pregnancy and Childbirth.," vol. 11(1), pp. 22–26, 2009.

[42] M. M. A. & A. Ghwass, "Prevalence and predictors of 6-month exclusive breastfeeding in a rural area in Egypt. Breastfeeding Medicine.," vol. 6(4), pp. 191–196, 2011.

[43] D. CL., "The breastfeeding self-efficacy scale: psychometric assessmentof the short form. J ObstetGynecol Neonatal Nurs.," vol. 32(6), pp. 734–744.

[44] T. Yeneabat, T. Belachew, and M. Haile, "Determinants of cessation of exclusive breastfeeding in Ankesha Guagusa Woreda , Awi Zone , Northwest Ethiopia : a cross-sectional study," pp. 1–12, 2014.

[45] R. Duchateau, L., Janssen, P., Lindsey, P., Legrand, C., Nguti, R. Sylvester, *The shared frailty model and the power for heterogeneity tests in multicenter trials, Computational Statistics Data Analysis, 40* . 2002.

[46] P. M. Therneau, T.M. and Grambsch, . "Extending the Cox model. Springer Verlag, New York.," in *Modeling survival data*, 2000.

[47] R. E. Beard, *Note on some mathematical mortality models. In: The lifespan of animals. Ciba colloquium on Aging, G.E.W. Wolstenholme and M. O'Connor (eds). Little, Brown, Boston,* . 1959.

[48] K. Rockwood, *Frailty and its definition: a worthy challenge. J. Am. Geriatr. Soc. 53.*2005.

[49] M. Gillick, *Pinning down frailty. J. Gerontol. Ser. A-Biol. Sci. Med. Sci. 56.* 2001.

[50] S. Podsiadlo, D. and Richardson, *The timed up and go — a test of basic functional mobility for frail elderly persons. J. Am. Geriatr. Soc. 39,* . 1991.

[51] E. Vaupel, J.W., Manton, K.G. and Stallard, *The impact of heterogeneity in individual frailty on the dynamics of mortality.* 1979.

[52] E. Vaupel, J.W., Manton, K.G. and Stallard, *The impact of heterogeneity in individual frailty on the dynamics of mortality. Demography 16,* . 1979.

[53] A. Wienke, *Frailty Models.Max Planck InstitutfrdemograscheForschungWorking Paper.*2003.

[54] S. Liang, K.Y., Self, S.G., Bandeen-Roche, K. and Zeger, *Some recent developments for regression analysis of multivariate failure time data. Lifetime Data Anal. 1,* . 1995.

[55] T. T. Pankratz VS, de Andrade M, *Random-effects Cox proportional hazard model: general variance components*. .

[56] Stave Bennet, *Analysis of survival data by the proportional odds model.* 1983.

[57] Central Statistical Agency [Ethiopia] and ICF International. Ethiopians Water Sector Development Program., 2016.

[58] A. W. Kasahun, W. G. Wako, M. W. Gebere, and G. H. Neima, “Predictors of exclusive breastfeeding duration among 6 – 12 month aged children in gurage zone , South Ethiopia : a survival analysis,” pp. 1–9, 2017.

[59] A. Emmanuel, “A Literature Review of the Factors That Influence Breastfeeding :,” *Int. Nurs. Heal. Sci.*, vol. 2, no. 3, pp. 28–36, 2015.

[60] “Applied Survival Analysis Regression modeling of time to event.pdf.” .

[61] Y. Q. Cui, S.F. and Sun, *Checking for the gamma frailty distribution under the marginal proportional hazards frailty model. Stat. Sin. 14,*. 2004.

[62] Z. Zhang, “Semi-parametric regression model for survival data : graphical visualization with R,” vol. 4, no. 23, pp. 1–8, 2009.

[63] S. T. Nielsen GG, Gill RD, Andersen PK, “A counting process approach to maximum likelihood estimation of frailty models. Scandinavian Journal of Statistics ; 19:.,” vol. 19, pp. 25–43, 1992.

[64] E. LE Zhi X, Grambsch PM, “Likelihood Ratio Test for the Variance Componentin a Semi-Parametric Shared Gamma Frailty Model." Research Report.,” vol. 5, 2005.

[65] C. A. McGilchrist, *REML estimation for survival models with frailty. Biometrics 49,*.1993.

[66] P. Duchateau, L. and Janssen, “The Frailty Model. New York, Springer.,” 2008.

[67] Y. YF, “Survival Analysis Final Report: Data Analysis For The SequentialPrimary Biliary Cirrhosis Data. Computational Statistics and Data Analysis 53:,” 2011.

[68] S. GE, “Estimating the Dimension of a Model. Annals of Statistics,” *6*, p. 461–464., 1978.

[69] K. RW, “On Some Criteria for Estimating the Order of a Markov Chain.Technometrics,” vol. 23, pp. 243–249, 1981.

[70] R. T. Kimbro, “On-the-job moms: work and breast feedinginitiation and duration for a sample of low-income women Maternal and Child Health Journal.,” vol. 10(1), pp. 19–26, 2006.

[71] K. L. Tan, “Factors associated with exclusive breastfeeding among infants under six months of age in peninsular Malaysia. Int Breastfeed J.,” *6(2)*, pp. 1–7, 2011.

[72] T. A. Ogunlesi, “Maternal socio-demographic factors influencing the initiation and exclusivity of breastfeeding in a Nigerian semi-urban setting. Maternal and Child HealthJournal.,” vol. 14(3), pp. 459–465, 2010.

[73] C. Wilhelm, S.L., Rodehorst, T.K., Stepans, M.B.F., Hertzog, M. &Berens, “Influence of intention and self-efficacy levels on duration of breastfeeding for midwest rural mothers.Applied Nursing Research.,” vol. 21(3), pp. 123–130, 2008.

[74] C. W. Li, L., Zhang, M., Scott, J.A. &Binns, “Factors associated with the initiation and duration of breastfeeding by Chinese mothers in Perth, Western Australia. Journal of Human Lactation: ” vol. 20(2), pp. 188–195, 2004.

Appendixes

Table A1: Schoenfield test for hazard proportional assumption of Ethiopian Demographic and Health Survey, 2016

Covariates Descripption	*Rho*	*Ch-square*	*P- value*
Mothers' age group			
15-19 (ref)			
20-24	*0.003723*	*4.64e-02*	*8.30e-01*
25-29	*0.015545*	*8.08e-01*	*3.69e-01*
30-34	*0.012598*	*5.27e-01*	*4.68e-01*
35-39	*0.006461*	*1.39e-01*	*7.09e-01*
40-44	*0.038718*	*4.91e+00*	*2.67e-02*
45-49	*0.053967*	*9.59e+00*	*1.96e-03*
Mothers' residence			
Rural (ref)			
Urban	*-0.005473*	*1.01e-01*	*7.51e-01*
Mothers' Education level			
No education (ref)			
Primary	*-0.030188*	*2.99e+00*	*8.36e-02*
Secondary	*-0.047451*	*7.85e+00*	*5.10e-03*
Higher	*-0.043026*	*6.40e+00*	*1.14e-02*
Family wealth index			
Poorest (ref)			
Poorer	*0.007417*	*1.80e-01*	*6.71e-01*
Middle	*0.039652*	*5.24e+00*	*2.21e-02*
Richer	*0.020095*	*1.32e+00*	*2.50e-01*
Richest	*-0.003061*	*3.13e-02*	*8.60e-01*
Children gender			
Male (ref)			
Female	*-0.004897*	*8.05e-02*	*7.77e-01*
Mothers current work			

No (ref)			
Yes	*0.046523*	*7.32e+00*	*6.81e-03*
Mothers' religion			
Orthodox (ref)			
Catholic	*0.026629*	*2.37e+00*	*1.24e-01*
Protestant	*0.014432*	*6.75e-01*	*4.11e-01*
Muslim	*-0.002672*	*2.48e-02*	*8.75e-01*
Traditional	*0.017234*	*9.85e-01*	*3.21e-01*
Others	*-0.036322*	*4.47e+00*	*3.45e-02*
Mothers visited by health worker			
No (ref)			
Yes	*-0.024324*	*1.99e+00*	*1.58e-01*
Husband Education level			
No education (ref)			
Primary	*0.003249*	*3.59e-02*	*8.50e-01*
Secondary	*0.005770*	*1.11e-01*	*7.39e-01*
Higher	*0.006186*	*1.27e-01*	*7.22e-01*
Don't know	*0.00828*	*2.31e-03*	*9.62e-01*
Mothers' family planning use			
Currently using (ref)			
Used since last birth	*0.004956*	*8.16e-02*	*7.75e-01*
Used before last birth	*-0.168455*	*9.14e+01*	*1.15e-21*
Never used	*-0.165927*	*8.77e+01*	*7.66e-21*
Mothers ANC visit			
No(ref)			
Yes	*0.017335*	*9.79e-01*	*3.22e-01*
Global	*NA*	*2.09e+02*	*1.08e-24*

Table A2; Multivariate Analysis using marginal cox model for EDHS 2016 data set.

Parameter Description	*Coefficient*	*Hazard Ratio*	*SE*	*Ex 95% CI*
Mothers Age group				
15-19 (ref)				
20-24	***-0.19895***	***0.8196***	***0.07460***	***(0.7081 0.9486)***
25-29	***-0.26622***	***0.7663***	***0.07423***	***(0.6625 0.8863)***
30-34	***-0.31664***	***0.7286***	***0.07777***	***(0.6256 0.8486)***
35-39	***-0.29148***	***0.7472***	***0.08247***	***(0.6356 0.8782)***
40-44	***-0.47158***	***0.6240***	***0.10722***	***(0.5057 0.7699)***
45-49	***-0.63065***	***0.5322***	***0.17892***	***(0.3748 0.7558)***
Mothers' residential				
Urban (ref)				
Rural	***0.04683***	***1.0479***	***0.05098***	***(0.9483 1.1581)***
Education status				
No education (ref)				
Primary	***0.03722***	***1.0379***	***0.04276***	***(0.9545 1.1286)***
Secondary	***0.06438***	***1.0665***	***0.07022***	***(0.9294 1.2238)***
Higher	***0.05276***	***1.0542***	***0.09922***	***(0.8679 1.2805)***
Mothers' work status				
No (ref)				
Yes	***-0.17693***	***0.8378***	***0.04055***	***(0.7738 0.9071)***
Mothers' visited by HW				
No (ref)				
Yes	***0.11610***	***1.1231***	***0.03711***	***(1.0443 1.2078)***
Contraceptive use				
Currently using (ref)				
Used since last birth	***-0.48857***	***0.6135***	***0.12414***	***(0.4810 0.7825)***
Used before last birth	***0.54025***	***1.7164***	***0.05377***	***(1.5448 1.9072)***
Never used	***0.24443***	***1.2769***	***0.04379***	***(1.1719 1.3913)***
ANC visit				
No (ref)				
Yes	***-0.09848***	***0.9062***	***0.04082***	***(0.8365 0.9817)***

Table **A3 lognormal frailty univariable Analysis for EDHS 2016 data set**

Covariate categories	coefficient	Exponentiated coefficient	SE	P value	95% CI
Age group					
15-19 (ref)					
20-24	-0.2034	0.8160	0.07353	5.7e-03	(0.7065 0.9425)
25-29	-0.2466	0.7815	0.07240	6.6e-04	(0.6781 0.9006)
30-34	-0.2911	0.7474	0.07471	9.7e-05	(0.6456 0.8653)
35-39	-0.2460	0.7819	0.07945	2.0e-03	(0.6692 0.9137)
40-44	-0.4081	0.6649	0.10456	9.5e-05	(0.5417 0.8161)
45-49	-0.5436	0.5806	0.17713	2.1e-03	(0.4103 0.8216)
Residence					
Urban (ref)					
Rural	0.104	1.11	0.04198	0.013	(1.022 1.205)
Mothers' Education level					
No education (ref)					
Primary	0.06659	1.0689	0.03879	0.086	(0.9906 1.153)
Secondary	0.03386	1.0344	0.08976	0.590	(0.9146 1.170)
Higher	-0.09896	0.9058	0.06285	0.270	0.7597 1.080
Family wealth index					
Poorest (ref)					
Poorer	-0.07959	-0.03121	0.9124	0.120	(0.8362 1.020)
Middle	-0.06228	0.9396	0.05368	0.25	(0.8458 1.044)
Richer	-0.03121	0.9693	0.05568	0.580	(0.8691 1.081)
Richest	-.09172	0.9124	0.04750	0.054	(0.8312 1.001)
Mothers' religion					
Orthodox (ref)					
Catholic	-0.181732	0.8338	0.21217	0.390	(0.5501 1.264)
Protestant	0.077398	1.0805	0.05685	0.170	(0.9665 1.208)
Muslim	-0.006303	0.9937	0.04574	0.890	(0.9085 1.087)
Traditional	-0.150375	0.8604	0.17619	0.390	(0.6091 1.215)
Others	-0.066527	0.9356	0.19041	0.730	(0.6442 1.359)
Current work status					
No (ref)					
Yes	-0.2058	0.814	0.03913	1.4e-07	(0.7539 0.8788)
Husband education level					
No education (ref)					
Primary	0.05960	1.0614	0.03885	0.12	(0.9836 1.145)
Secondary	-0.03465	0.9659	0.05754	0.55	(0.8629 1.081)
Higher	-0.01784	0.9823	0.06321	0.78	(0.8679 1.112)
Don't know	0.25847	1.2950	0.19076	018	(0.8910 1.882)

Mothers' visited by HW						
No (ref)						
Yes	**.1018**	**1.107**	**0.03584**	**0.03584**	**(1.032**	**1.188)**
ANC visit						
No (ref)						
Yes	**-0.08318**	**0.9202**	**0.03789**	**0.28**	**(0.8543**	**0.9911)**
Children gender						
Male (ref)						
Female	**-0.004137**	**0.9959**	**0.0335**	**0.90**	**(0.9326**	**1.063)**
Contraceptive use						
Currently using (ref)						
Used since last birth	**-0.4853**	**0.6155**	**0.12401**	**9.1e-05**	**(0.4827**	**0.7849)**
Used before last birth	**0.4763**	**1.6101**	**0.05219**	**7.1e-20**	**(1.4535**	**1.7835)**
Never used	**0.1874**	**1.2061**	**0.04204**	**8.3e-06**	**(1.1107**	**1.3097)**

Table A4; Multivariate Analysis using cox stratified model for EDHS 2016 data set.

Parameter Description	*Coefficient*	*Relative risk*	*SE*	*P value*
Mothers Age group				
15-19 (ref)				
20-24	***-0.204***	***0.816***	***0.075***	***0.000***
25-29	***-0.270***	***0.764***	***0.075***	***0.000***
30-34	***-0.316***	***0.729***	***0.079***	***0.000***
35-39	***-0.309***	***0.734***	***0.084***	***0.000***
40-44	***-0.480***	***0.619***	***0.108***	***0.000***
45-49	***-0.631***	***0.532***	***0.180***	***0.000***
Mothers' residential				
Urban (ref)				
Rural	***-0.028***	***0.972***	***0.057***	***0.619***
Education status				
No education (ref)				
Primary	***0.037***	***1.038***	***0.044***	***0.405***
Secondary	***0.085***	***1.089***	***0.073***	***0.244***
Higher	***0.078***	***1.081***	***0.103***	***0.448***
Mothers' work status				
No (ref)				
Yes	***-0.205***	***0.815***	***0.042***	***0.000***
Mothers' visited by HW				
No (ref)				
Yes	***0.107***	***1.113***	***0.038***	***0.005***
Contraceptive use				
Currently using (ref)				
Used since last birth	***-0.478***	***0.620***	***0.125***	***0.000***
Used before last birth	***0.573***	***1.773***	***0.125***	***0.000***
Never used	***0.275***	***1.317***	***0.047***	***0.000***

ANC visit				
No (ref)				
Yes	***--0.111***	***0.895***	***0.042***	***0.008***

Appendix A5, Multivariate Analysis using lognormal shared frailty for EDHS 2016 data set

Covariates Description	***coefficients***	***Hazard Ratio***	***SE***	***95% CI***
Mothers' age group				
15-19(ref)				
20-24	***-0.20110***	***0.8178***	***0.07466***	***(0.7065 0.9467)***
25-29	***-0.26945***	***0.7638***	***0.07447***	***(0.6601 0.8838)***
30-34	***-0.32075***	***0.7256***	***0.07808***	***(0.6226 0.8456)***
35-39	***-0.29761***	***0.7426***	***0.08289***	***(0.6312 0.8736)***
40-44	***-0.47824***	***0.6199***	***0.10758***	***(0.5020 0.7654)***
45-49	***-0.64197***	***0.5263***	***0.17919***	***(0.3704 0.7477)***
Residence				
Urban(ref)				
Rural	***0.01715***	***1.0173***	***0.05356***	***(0.9159 1.1299)***
Educational status				
No education(ref)				
Primary	***0.03527***	***1.0359***	***0.04352***	***(0.9512 1.1281)***
Secondary	***0.07204***	***1.0747***	***0.07159***	***(0.9340 1.2366)***
Higher	***0.05927***	***1.0611***	***0.10042***	***(0.8715 1.2919)***
Work status				
No(ref)				
Yes	***-0.18792***	***0.8287***	***0.04095***	***(0.7648 0.8979)***
Visited by HW				
No(ref)				
Yes	***0.11231***	***1.1189***	***0.03748***	***(1.0396 1.2042)***
Contraceptive use				
Currently using(ref)				
Since last birth	***-0.48394***	***0.6164***	***0.12427***	***(0.4831 0.7863)***
Before last birth	***0.54770***	***1.7293***	***0.05405***	***(1.5554 1.9225)***
Never used	***0.25591***	***1.2916***	***0.04542***	***(1.1816 1.4119)***
Antenatal care visit				

No(ref)				
Yes	*-0.10173*	*0.9033*	*0.04125*	*(0.8331 0.9793)*

Appendix A6, Multivariate Analysis using shared Gaussian frailty model for EDHS 2016 data set

Covariate categories	*Coefficients*	*Hazard ratio*	*SE*	*P value*
Age group				
15-19 (ref)				
20-24	*-0.20117859*	*0.8177664*	*0.07466301*	*7.0e-03*
25-29	*-0.26955700*	*0.7637177*	*0.07446509*	*2.9e-04*
30-34	*-0.32089399*	*0.7255002*	*0.07807675*	*4.0e-05*
35-39	*-0.29787517*	*0.7423940*	*0.08288064*	*3.3e-04*
40-44	*-0.47849604*	*0.6197147*	*0.10757305*	*8.7e-06*
45-49	*-0.64242744*	*0.5260140*	*0.17918175*	*3.4e-04*
Residence				
Urban(ref)				
Rural	*0.01575623*	*1.0158810*	*0.05357540*	*7.7e-01*
Education level				
No education(ref)				
Primary	*0.03521443*	*1.0358418*	*0.04349759*	*4.2e-01*
Secondary	*0.07239964*	*1.0750849*	*0.07160386*	*3.1e-01*
Higher	*0.05966235*	*1.0614781*	*0.10044748*	*5.5e-01*
Mothers' current work status				
No (ref)				
Yes	*-0.18840113*	*0.8282824*	*0.04095069*	*4.2e-06*
Mothers visited by HW				
No (ref)				
Yes	*0.11212307*	*1.1186505*	*0.03747232*	*2.8e-03*
Pattern of contraceptive use				
Currently using (ref)				
Used after last birth	*-0.48374274*	*0.6164718*	*0.12427198*	*1.6e-08*
Used before last birth	*0.54799907*	*1.7297884*	*0.05404213*	*0.0e+00*
Never used	*0.25637529*	*1.2922376*	*0.04537725*	*1.6e-08*

ANC visit				
No (ref)				
Yes	***-0.10186024***	***0.9031558***	***0.04123132***	***1.3e-02***

Table A7: Parameter Estimates (SE) for Overall survival for EDHS 2016 data set

Covariate description	***Gamma frailty***	***Lognormal frailty***	***Cox stratified***
Parameter	***Estimate (SE)***	***Estimate(SE)***	***Estimate(SE)***
Age group			
15-19(ref)			
20-24	***0.07465***	***0.07466***	***0.075***
25-29	***0.07443***	***0.07447***	***0.075***
30-34	***0.07803***	***0.07808***	***0.079***
35-39	***0.08281***	***0.08289***	***0.084***
40-44	***0.10751***	***0.10758***	***0.108***
45-49	***0.17914***	***0.17919***	***0.180***
Residence			
Urban(ref)			
Rural	***0.05304***	***0.05356***	***0.057***
Mothers' education level			
No education(ref)			
Primary	***0.04338***	***0.04352***	***0.044***
Secondary	***0.07134***	***0.07159***	***0.073***
Higher	***0.10017***	***0.10042***	***0.103***
Current mother work status			
No(ref)			
Yes			
	0.04087	***0.04095***	***0.042***
Visited by HW			
No(ref)			
Yes	***0.03741***	***0.03748***	***0.038***
Antenatal care visit			
No(ref)			
Yes	***0.04118***	***0.04125***	***0.042***
Contraceptive use pattern			
Currently using(ref)			
Used since last birth	***0.12425***	***0.12427***	***0.125***
Used before last birth	***0.05400***	***0.05405***	***0.125***
Never used	***0.04511***	***0.04542***	***0.047***

Appendix, Multivariate Analysis using t shared frailty for EDHS 2016 data set

Covariates Description	***coefficients***	***Hazard Ratio***	***SE***	***95% CI***
Mothers' age group				
15-19(ref)				
20-24	***-0.20301***	***0.8163***	***0.07473***	***(0.7050 0.9450)***
25-29	***-0.27138***	***0.7623***	***0.07474***	***(0.6585 0.8826)***
30-34	***-0.32345***	***0.7375***	***0.07845***	***(0.6205 0.8439)***
35-39	***-0.30446***	***0.6164***	***0.08340***	***(0.6263 0.8685)***
40-44	***-0.48380***	***0.5202***	***0.10806***	***(0.4988 0.7619)***
45-49	***-0.65349***	***0.9742***	***0.17946***	***(0.3660 0.7395)***
Residence				
Urban(ref)				
Rural	***-0.02615***	***1.0350***	***0.05750***	***(0.8704 1.0904)***
Educational status				
No education(ref)				
Primary	***0.03438***	***1.0866***	***0.04434***	***(0.9488 1.1289)***
Secondary	***0.08301***	***1.0773***	***0.07340***	***(0.9410 1.2547)***
Higher	***0.07446***	***0.8180***	***0.10252***	***0.8812 1.3171***
Work status				
No(ref)				
Yes	***0.20095***	***0.8180***	***0.04144***	***(0.8812 1.3171)***
Visited by HW				
No(ref)				
Yes	***0.10661***	***1.1125***	***0.03792***	***(1.0328 1.1983)***
Contraceptive use				
Currently using(ref)				
Since last birth	***-0.47806***	***0.6200***	***0.12442***	***(0.4858 0.7912)***
Before last birth	***0.55542***	***1.7427***	***0.05430***	***(1.5667 1.9384)***
Never used	***0.26787***	***1.3072***	***0.04733***	***(1.1914 1.4342)***
Antenatal care visit				
No(ref)				
Yes	***-0.10533***	***0.9000***	***0.04166***	***(1.1914 1.4342)***