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Determinants of Under-Five Mortality in Ethiopia: An Application of Cox Proportional Hazard and Frailty Models

Etiyopya'da Beş Yaş Altı Ölümlerin Belirleyicileri: Cox Orantısal Hazard ve Kırılganlık Modellerinin Uygulaması

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ABSTRACT **Objective:** Under-five mortality is an essential indicator of the development of a country. In Ethiopia under-five mortality rate is among the highest in the world. Nearly one out of 10 babies born in Ethiopia does not survive to celebrate its first birthday. **Material and Methods:** The data for the study was obtained from Ethiopian Demography and Health Survey data conducted in 2016. The Kaplan-Meier, Cox'sproportional hazards and gamma shared frailty models were employed for the analysis of under-five children data. **Results:** Results obtained by fitting both Cox-proportional hazard model and gamma shared frailty model: place of residence, Type of Birth, Birth order, sex of a child and preceding birth intervalwere found to be significant factors. Further more a high risk death of under-five children was found to be associated with place of residence at rural, multiple births, birth order at fifth and above, male children and preceding birth interval less than 24 months. From gamma shared frailty model (**θ=0.145**) we had enough evidence that the existence of unobserved heterogeneity at the regional level. **Conclusion:** The findings of this paper highlighted the potential associated with under-five child mortality in Ethiopia. The shared frailty model provided better estimates and also justified the presence of unobserved heterogeneity at regional level. Therefore, special attention should be given to these significant predictors, which ultimately reduce the under-five mortality.

Keywords: Under-five mortality; Kaplan Meier; proportional hazards model; gamma frailty; survival

ÖZET Amaç: Beş yaş altı ölüm, bir ülkenin gelişiminde temel bir göstergedir. Etiyopya'da doğan neredeyse 10 bebekten biri ilk doğum gününü kutlayana kadar hayatta kalamamaktadır. **Gereç ve Yöntemler:** Çalışma verisi 2016 yılında yürütülen Etiyopya Demografi ve Sağlık Çalışması'ndan elde edilmiştir. Kaplan-Meier, Cox orantısal hazard modeli ve gamma kırılganlık modelleri beş yaş altı çocuklara ait verinin analizinde kullanılmıştır. **Bulgular:** Hem Cox orantısal hazard modeli hem de gamma kırılganlık modeli uygulanarak elde edilen sonuçlar: ikamet yeri, doğum tipi, doğum sırası, çocuğun cinsiyeti ve önceki doğum aralığı anlamlı faktörler olarak bulunmuştur. Ayrıca beş yaş altı çocuklardaki yüksek ölüm riskinin kırsal ikamet yeri, çoklu doğum, beş ya da daha fazla doğum sırası, erkek çocuk ve önceki doğum aralığının 24 aydan az olması ile ilişkili olduğu bulunmuştur. Gamma kırılganlık modelinden (**θ=0.145**) bölgesel düzeyde gözlenmeyen heterojenliğin varlığına dair yeterli kanıt elde edilmiştir. **Sonuç:** Bu makalenin bulguları Etiyopya'daki beş yaş altı çocuk ölümleri ile ilişkili potansiyeli vurgulamıştır. Kırılganlık modeli daha iyi tahminler sağlamış ve bölgesel düzeyde gözlenmeyen heterojenliği doğrulamıştır. Bu nedenle, beş yaş altı ölümü azaltmak için bu faktörlere özel ilgi verilmelidir.

Anahtar Kelimeler: Beş yaş altı ölüm; Kaplan Meier; orantısal hazard modeli; gamma kırılganlık; sağkalım

The under-five mortality rate (U5MR) is that the likelihood (expressed as a rate per a thousand live births) of a child born during a specific year dying before reaching the age of five if subject to current age-specific mortality rates. An annual report by the United Nation Inter-agency Group for Child Mortality Estimation showed that in 2011, an estimated 6.9 million children died before their fifth birthday.[1,2]

The twentieth century witnessed dramatic decline in under-five mortality in the majority countries of the world, despite initial levels, socio-economic circumstances and development ways. However, more than 10.8 million children younger than 5 years die once a year principally from preventable causes. Six countries accounted for 50% of worldwide deaths in children younger than five and forty two countries for ninety percent.[3] Child mortality varies among world regions, and these differences are becoming wide. In 2000, there have been 175 deaths per one thousand live births in Sub Saharan Africa and solely 6 per one thousand within the industrial countries, that could be a twenty nine fold difference.[3,4]

As of the EDHS report, child mortality rate in Ethiopia was declined from 166 per thousand in 2005 to eighty eight per thousand deaths in 2011.[5] For the five years before the survey, the death rate was fifty nine per a thousand live births, the child mortality rate was thirty one per one thousand children surviving to age 1 year, and the under-five mortality rate was eighty eight per one thousand live births. This leads that one in seventeen Ethiopian children dies before the first birthday and one in eleven Ethiopian children dies before the fifth birthday.

In 2000, as part of the millennium development goals for health, nations pledged to ensure a two third reduction in child mortality with 2015, from the base year 1990.[6] To attain these goals, understanding of determinants of under-five mortality and imposing remarkable intervention is anticipated from each country of the world. Determinants of mortality can be depicted the usage of conceptual framework developed. This framework consisted of socio economic and proximate determinants.[7] The socio-economic determinants such as income, social reputation and education circuitously affect under-five mortality through the operation of proximate determinants of maternal factors like age, parity, birth order etc.., and as well as environmental, nutritional, injury and behavioral factors *(Abdulkarimova U. Frailty models for modelling heterogeneity. McMaster University; 2013. p.73).* Therefore, Survival analysis consists in determining study subjects survival when exposed to the variables considered risk factors. It is presently recognized that the study of risk factors for infant mortality is very important, as, specifically in the newborn, it can be considered one of the best quality indicators for health care, as well as an indicator for population social and economic welfare.[8]

MATERIAL AND METHODS

This study provides an extension of Cox model to frailty model that analyse the factors affecting under-five child mortality in Ethiopia taking into account any extra heterogeneity present in the data. Few authors have tried to determine the factors associated with child mortality in Ethiopia using Cox proportional hazard model. No one has taken into consideration of unobserved heterogeneity in the data. Therefore we have employed a share frailty model to investigate the potential factors associated with under-five child mortality taking into account the heterogeneity at regional level. The frailty term takes into consideration the situation where some of the children may be exposed to the hazard of death before five years were more than the others. Moreover, we have used the recent available Ethiopian Demographic and Health Survey-2016 data.Therefore this study sets out to provide a comprehensive insight into these factors using Kaplan Meier for comparing survivor; Cox model with gamma frailty to account any extra heterogeneity in the data and consequently it may help as a guide to health care personnel to reduce the under-five child mortality.

DATA, SAMPLING AND DESIGN WEIGHTS

The data for the analysis was culled from Ethiopian Demographic and Health Survey (EDHS 2016). The EDHS is at national level, population-based, cross-sectional survey followed a complex sampling design with region and residence as strata. The first stage of the selection were 645 PSU with 202 EAs urban and 443 EAs rural areas based on the 2007 Ethiopian Population and housing Census (PHC) conducted by Ethiopian Central statistics Agency (CSA). A total of 18,008 households were considered, of which 16,650 (98% of response rate) households were eligible. The women were interviewed by distributing questioners and information on their birth history and 9072 births were considered for this study (the EDHS 2016 can be accessed on request through proper format).

VARIABLES IN THE STUDY

The response variable: The response variable for this study is length of time (survival time in months) from date of birth to date of death or censor (if the child survives for the past 59 months).

Covariates: The covariates that are expected to affect the survival of under-five children were classified as; Social demographic (Mother's age at first birth; Sex of household head); social economic (economic status of the family; Mother's educational level); environmental (Source of drinking water; Type of place of residence) and proximate or biological (Type of birth (multiple or single birth); Sex of the child; birth order; Previous birth interval).

Methods Used: The Kaplan-Meier product limit estimation method has been used for survival estimation of under-five children. Log rank test has been used to examine the significance in survival probability for various categories. Cox Proportional Hazard and shared frailty model have been used to determine the significant variables associated with child mortality. The detail of methods used has been discussed below.

Survival Data Analysis: It is a collection of statistical procedures for data analysis for which the outcome variable of interest is time until an event occurs (time-to-event data), which is always nonnegative and has a positively skewed distribution.[9]

The Survival Function: Let T be a random variable, which can take any non-negative value, associated with the actual survival times, t (time of death). When the random variable T has a probability distribution with underlying probability density function $f(t)$, the distribution function (cumulative distribution function) of T is given by:

$$F(t) = P(T < t) = \int_0^t f(u)\, du \quad t \geq 0 \tag{1}$$

Which represents the probability that a subject selected at random will have a survival time less than some stated value t. Then, the survival function $S(t)$ is defined as:

$$S(t) = P(T \geq t) = 1 - F(t) \tag{2}$$

The survivor function can therefore be used to represent the probability that an individual survives from the time origin to sometime beyond t.

The Hazard Function: The hazard function is widely used to express the risk or hazard of experiencing the event at some time t, and is obtained from the probability that an individual experiencing the event at time t, conditional on he or she has survived to that time. That is, the function represents the instantaneous failure rate for an individual surviving to time t.

The hazard function **h(t)** is defined by:

$$h(t) = \lim_{\Delta t \to 0} \frac{P(t < T < t + \Delta t / T \geq t)}{\Delta t} \tag{3}$$

Cox proportional hazard model: Cox proportional hazard model is one of the most popular models in survival analysis, which is used to assess the covariate effects on hazard function. The model is given by

$$h(t, X_i, \beta) = h_0(t)\exp(\beta' X_i) \tag{4}$$

where $h_o(t)$ is the baseline hazard function which is obtained all X's are set to zero, X_i is the vector of values of the explanatory for the i^{th} children at time t and $\beta = (\beta_1, \beta_2, \ldots\ldots\beta_p)^T$ is the vector of unknown regression parameters that are assumed to be the same for all the children in the study, which measures the influence of the covariate on the survival experience. An attractive property of the Cox model is that, even though the baseline hazard part of the model is unspecified, it is still possible to estimate the β's in the exponential part of the model. So, it can equally be regarded as linear model, as a linear combination of the variables for the logarithm transformation of the hazard ratio given by

$$\log\left(\frac{h(t, X_i, \beta)}{h_0(t)}\right) = \log\left(\exp^{\beta X}\right) = \beta X' = \beta_1 X_1 + \beta_2 X_2 + \ldots + \beta_p X_p \tag{5}$$

The quantity $\beta' X = \beta_1 X_1 + \beta_2 X_2 + \ldots\ldots + \beta_p X_p$ is called the linear combination of the Cox proportional hazards model. The hazard function in the Cox model is called semi-parametric function since it does not explicitly describe the baseline hazard function, $h_o(t)$. The survival function of the proportional hazard model is estimated as:

$$S(t, X, \beta) = \exp^{-H(t, \beta X)} \tag{6}$$

Where $H(t, X, \beta)$ is the cumulative hazard function at time t for a subject with covariate x. Since we have assumed that survival time is absolutely continuous, the value of the cumulative hazard function is expressed as:

$$H(t, X, \beta) = H_0(t)\exp(\beta' X) \tag{7}$$

Consequently, from the proportional hazards function, we obtained the survivor function given by:

$$S(t, X, \beta) = [S_0(t)]^{\exp(\beta X)} \tag{8}$$

Where: $H_o(t)$ is the baseline cumulative hazard function and $S_o(t)$ is the baseline survival function.[9] The $\beta' s$ unknown parameters can be estimated by using partial likelihood approach.

Semi parametric frailty models: A frailty model is a hazard model with a multiplicative frailty factor. The major assumption of a frailty model is that the information about the hidden internal or external factors is contained in the shape and structure of the hazard function and in the form of the frailty distribution.[10] A univariate frailty model assumes a frailty term for each individual and this frailty term represents the individual's unmeasured or hidden variables after considering the measured variables.Suppose we have a sample of n children in our study. Some of these are fail earlier than others due to unobserved heterogeneity. The proportional hazards model assumes that conditional on the frailty, the hazard function for an individual at time t > 0 is

$$h_j(t, X_i, \beta) = h_o(t)\exp(\beta' X_j + W_j \phi),\ j = 1,2,\ldots\ldots\ldots n \tag{9}$$

Where, W_j is a frailty term from a probability distribution with a mean of 0 and variance of 1. If W_j could be measured and included in the model, then ϕ would go to 0 and we would obtain the standard proportional hazards model. The hazard function conditional on both variables and frailty can be rewritten as:

$$h_j(t, X_i, \beta) = h_o(t) U_j \exp(\beta' X_j + W_j \phi), j = 1,2,\ldots\ldots\ldots n \tag{10}$$

Where, $U_j = \exp(W_j \phi)$. This shows that the hazard of an individual also depends on an unobservable random variable, U_j, which acts multiplicatively on the hazard rate. If frailty is not taken into account, then $U_j = 1$.

Shared frailty model is similar to the individual frailty model except the only difference is that frailty is now shared among the n_i observations in the i^{th} group. This model was introduced by observed that individuals in the same cluster are assumed to share the same frailty and this is the reason why it is called the shared frailty model.[10-14] Frailty is assumed to be independent across the groups or clusters while the survival times of individuals within the same group are conditionally dependent. Suppose we have j observations and i subgroups.

Each subgroup consists of n_i observations and $\sum_{i=0}^{G} n_i = N$, where N is the total number of individuals under study. The hazard rate for the j^{th} individual in the i^{th} subgroup is given by:

$$h_{ij}(t, X_{ij}, \beta) = h_o(t) U_j \exp(\beta' X_{ij} + W_j \phi), i = 1,2,\ldots\ldots\ldots, G, j = 1,2,\ldots . n_i \tag{11}$$

Where, W_i are frailty terms for subgroups and their distribution is again assumed to be independent with a mean of 0 and a variance of 1. The hazard function conditional on variables and frailties can be rewritten as:

$$h_{ij}(t, X_{ij}, \beta) = h_o(t) U_j \exp(\beta' X_{ij}), i = 1,2,\ldots\ldots\ldots, G, j = 1,2,\ldots . n_i \tag{12}$$

Where, $U_j = \exp(W_j \phi)$, are independent identically distributed following a chosen distribution, as in the univariate frailty models. The model assumes that the survival times are independent given the values of the frailties. The value of U_j is constant over time and common to all the under-five children in the same region and thus induces a within group dependence. Also the U_j is following some distribution with positive support with unit mean and variance Θ. The Gamma and inverse Gaussian distributions are most commonly used frailty distributions.

In this paper, we focus on the semi parametric gamma frailty distribution model. For simplicity, we restrict ourselves to a one parameter Gamma distribution.

GAMMA DISTRIBUTION

Suppose a random variable T > 0 is gamma distributed with scale parameter $\lambda > 0$ and shape parameter $\alpha > 0$, i.e. T~ Gamma (λ, α). The survival and hazard functions of the gamma distribution are given by:

$$S(t) = \frac{\Gamma(\alpha, \lambda t)}{\Gamma(\alpha)} \tag{13}$$

$$h(t) = \frac{\lambda^{\alpha} t^{\alpha-1} e^{-\lambda t}}{\Gamma(\alpha, \lambda t)} \tag{14}$$

Where, $\Gamma(\alpha, \lambda t)$ is the upper incomplete gamma function. The hazard function is decreasing, constant and increasing when $0 < \alpha < 1$, $\alpha = 1$ and $\alpha > 1$ respectively.

The gamma distribution is very well known and has simple densities. It is the most common distribution used for describing frailty. Even though gamma models do not have closed form expressions for survival and hazard functions, from a computational view, it fits well to frailty data and it is easy to derive the closed form expressions for unconditional survival and hazard functions. For this reason, this distribution is used often in most applications. Frailties appearing in the conditional likelihood can be integrated out and hence give simple expressions for marginal likelihood. Thus, it is easy to obtain parameter estimates by maximizing the marginal likelihood.

Many authors used the gamma frailty model such as for the duration of unemployment, to check the proportional hazards assumptions in the study of malignant melanoma and studies on population mortality data from Sweden.[11,15-16]

In gamma frailty models, the restriction $\alpha = \lambda$ is used, which results in expectation of 1.The variance of the frailty variable is then $\frac{1}{\lambda}$. Assume that the frailty term U is distributed as gamma with $E(U) = 1$ and $\mathrm{var}(U) = \theta$. Then $\lambda = \alpha = \frac{1}{\theta}$ The distribution function of the frailty term U is then one parameter gamma distribution, $U_i \sim Gamma(1/\theta, 1/\theta)$:

$$g(\theta) = \frac{u^{\frac{1}{\theta}-1} \exp^{\left(\frac{-u}{\theta}\right)}}{\Gamma\left(\frac{1}{\theta}\right) \theta^{\frac{1}{\theta}}} \tag{15}$$

Where $\theta > 0$ indicates the presence of heterogeneity, the large value of θ reflects a greater degree of heterogeneity.

MODEL COMPARISON

In order to compare proposed models we have used Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC).[17] The model with smaller AIC and BIC value is termed as better model.

RESULTS

The summary statistics of the variable selected for the study are reported in the Table 1,Among none educated mothers, from the total of 4928 children born 6.57% died before celebrating their fifth birthday which was the highest death proportion compared to other education levels of mothers. These were followed by mothers who completed primary education with 5.78% of the deaths. The category of mothers with the least percentage of deaths was those who had acquired secondary and higher education with 4.42% of deaths. Of the total live births, 6.86% and 5.02% of under-five death have occurred among the male and female, respectively. Children born as a result of multiple births recorded the highest percentage of death compared to those as a result of a single birth. Out of the 231 multiple born 20.86 % had died before the age of five and this was the highest proportion compared to those born out of a singleton birth which recorded 5.57% of the death. The majority of child (6.36 %) death occurred due to the mothers age at birth is less than 18 years. It is also found that 204 (9.63 %) child death is prevalent among the mothers having the birth interval less than 24 months. About 6.72 % under-five deaths attributed to mothers having children ever born is more than four. Also maximum number of under-five deaths 568 (6.55%) reported in the rural areas.

The overall Kaplan-Meier survivor l curve, Figure 1, indicated that the probability of children surviving was high at the first months that are relatively decreases as follow up time increases.

TABLE 1: Summary statistics of children under the age of five for selected variable included in the analysis.

Variables	Category	Total	Death (%)
Fathers education level	No education	4928	324 (6.57)
	Primary	3220	186 (5.78)
	Secondary & higher	1785	79(4.42)
Type of Birth	Single Birth	10363	577(5.57)
	Multiple (Twins)	278	58(20.86)
Sex of the child	Male	5483	376(6.86)
	Female	5158	259(5.02)
Type of place of residence	Urban	1974	67(3.39)
	Rural	8667	568(6.55)
Wealth index	Poor	5775	399(6.91)
	Middle	1466	80(5.46)
	Rich	3400	156(4.59)
Birth order number	1-2	3968	231(5.82)
	3-4	2860	153(5.35)
	5th +	3813	251(6.58)
Sex of household head	Male	8383	508(6.06)
	Female	2258	127(5.62)
Source of drinking water	Piped water	3133	143(4.56)
	Borehole	1481	91(6.14)
	Well	1713	124(7.24)
	Surface/Rain/pond	4135	259(6.26)
	Other	179	12(6.70)
Age at first birth	<=18	5282	336(6.36)
	>18	5359	299(5.58)
Children ever born	One child	1470	61(4.15)
	Two children	1807	89(4.93)
	Three children	1589	97(6.10)
	Four and more children	5775	388(6.72)
Type of toilet facility	Flush Toilet	422	14(3.32)
	Pit latrine	5289	286(5.41)
	No facility	4930	335(6.79)
Preceding birth interval	<24 months	2118	204(9.63)
	24-48 months	4368	211(4.83)
	>=48 months	1974	79(4.00)
Mothers education level	No education	6838	451(6.60)
	Primary	2678	140 (5.23)
	Secondary & higher	1125	44(3.911)

From the Log-rank test there was a significant variation in the death time of different categories of (P-value <0.05), except the father educational level, birth order, age at first birth and mother educational level (Table 2).

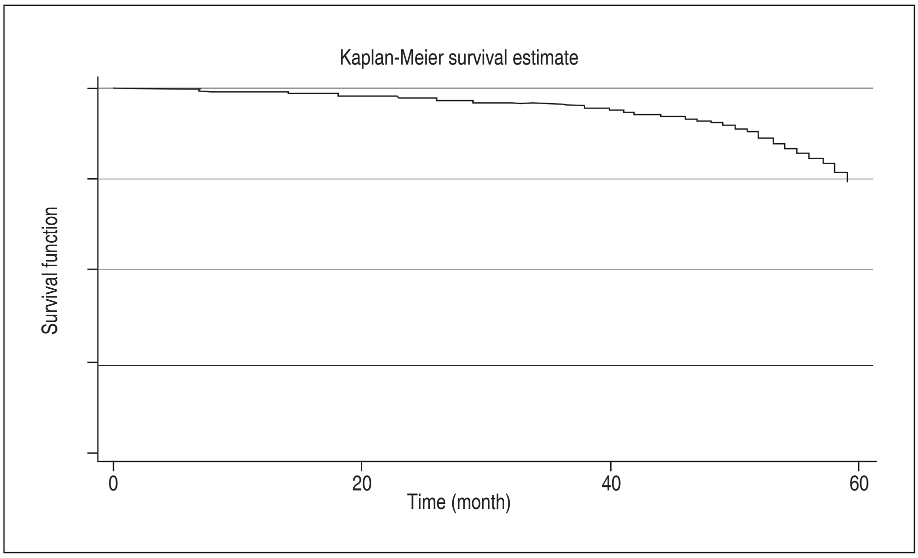

FIGURE 1: The overall estimate of Kaplan-Meier survivor function of the children under the age of five.

The Table 3 shows the estimated β's coefficients, standard error, hazard ratio (i.e., exp^β) and P-values of the Cox PH model. It shows that the viz., sex of a child, type of birth, birth order, place of residence and preceding birth interval were significantly associated with survival time of under-five children (p-value < 0.05). Sex of a child is found to be very important significant predictor of child survival, as it shows that female children were less likelihood to die as compared to male. Multiple birth children had approximately 4.480 times more risk of death as compared to children with singleton birth [HR=4.480, 95%CI; 3.296, 6.090].

Place of residence found to be significantly associated with the survival of under-five children. The hazard death of children born from mothers resided in rural was 1.699 [95% CI: 1.101, 2.620]. This means children born from mothers resided in rural were more likely to die than mothers resided in urban. Previous birth interval was another significant variable, a reduced risk of under-five child mortality by 58.7 and 66.9 percent for 24-48 and 48 and above months respectively as compared to children born less than 24

TABLE 2: Results of log-rank test of equality of survival distribution for the different categorical variables.

Variables	DF	Chi-square	P-value
Fathers education level	2	4.599	1.000
Type of Birth	1	116.826	0.000
Sex of the child	1	12.253	0.000
place of residence	1	23.110	0.000
Wealth index	2	20.900	0.000
Birth order number	2	4.910	0.086
Source of drinking water	4	15.890	0.003
Age at first birth	1	0.481	0.488
Type of toilet facility	2	14.894	0.001
Preceding birth interval	2	38.465	0.000
Mothers education level	2	4.719	0.094

TABLE 3: Final fitted Cox's Proportional Hazard Model of children under the age of five.

Variables		B	SE(B)	HR[95%CI]	P-Value
Father Education level	(No education)				
	Primary	-0.081	0.105	.923 [.738, 1.153]	0.479
	Secondary & Higher	0.016	0.183	1.016[.714, 1.446]	0.928
Type of Birth	(Single)				
	Multiple	1.505	0.698	4.503 [3.322, 6.103]	0.000
Sex of a child	(Male)				
	Female	-0.192	0.078	0.826[.686, .993]	0.042
Source of drinking water	(Piped)				
	Borehole	0.129	0.184	1.138[.828,1.564]	0.426
	Well	0.044	0.169	1.045[.762,1.434]	0.784
	Surface/Rain/Pond/ Lake	-0.020	0.134	0.981[.750,1.282]	0.886
	Others	0.201	0.522	1.223 [.530, 2.824]	0.638
Toilet facility	(Flush)				
	Pit latrine	-0.214	0.250	0.807[.440,1.483]	0.490
	No facility	-0.118	0.280	.889[.479, 1.650]	0.709
Birth order	(1-2)				
	3-4	-0.062	0.130	0.940[.716, 1.234]	0.655
	5+	0.047	0.141	1.048 [.805, 1.364]	0.727
Age at first birth	(<=18)				
	>18	-0.089	0.087	.915[.758, .1.104]	0.353
Wealth index	(Poor)				
	Medium	-0.208	0.124	0.812[0.602,1.095]	0.172
	Rich	-0.054	0.141	0.947[0.708, 1.268]	0.716
Mother Education level	(No education)				
	Primary	0.158	0.156	1.171[.902, .1.520]	0.237
	Secondary & Higher	0.247	0.365	1.281[.732, .2.240]	0.386
Place of residence	(Urban)				
	Rural	0.552	0.386	1.737 [1.123, 2.686]	0.013
Preceding Birth Interval	(below 24)				
	24-48	-0.572	0.058	.564 [.461, .691]	0.000
	48+	-0.552	0.082	.576 [.434, .762]	0.000

(# Categories shows in bracket as reference)

months after the previous birth. The hazard ratio of Children who had birth order fifth and above was 1.683 [95% CI: 1.190, 2.380]. This means children who born at the fifth and above were 1.683 times more likely to die than children born at 1^{st}-2^{nd} order.

Since it is possible to expect some correlation within a region, we have depicted this in (Table 4), as shared frailty model where sharing takes place on the regional level. The predictors' viz., type of birth, birth order, sex of a child, place of residence and preceding birth interval were found to be significant contributors in the survival of the under-five children while controlling for regional level effect. Note that shared frailty model estimates are quite similar to that of Cox proportional without frailty model. In this study we

TABLE 4: Final fitted Semi-parametric Gamma frailty Model of children under the age of five.

Variables		B	SE(B)	HR[95%CI]	P-Value
Father Education level	(No education)				
	Primary	-0.111	0.102	.896 [.715, 1.120]	0.329
	Secondary & Higher	0.010	0.182	1.010[.710, 1.437]	0.956
Type of Birth	(Single)				
	Multiple	1.500	0.702	4.480 [3.296, 6.090]	0.000
Sex of a child	(Male)				
	Female	-0.190	0.078	0.827[.688, .995]	0.044
Source of drinking water	(Piped)				
	Borehole	0.135	0.186	1.145[.832,1.574]	0.406
	Well	0.030	0.166	1.030[.751,1.414]	0.854
	Surface/Rain/Pond/ Lake	-0.027	0.133	0.9731[.745,1.272]	0.844
	Others	0.157	0.500	1.170 [.506, 2.703]	0.713
Toilet facility	(Flush)				
	Pit latrine	-0.234	0.245	0.791[.431,1.454]	0.451
	Others	-0.138	0.271	.871[.470, 1.616]	0.661
Birth order	(1-2)				
	3-4	0.164	0.176	1.179[.880, 1.579]	0.655
	5+	0.520	0.297	1.683 [1.190, 2.380]	0.003
Age at first birth	(<=18)				
	>18	0.106	0.119	1.112[.902, .1.370]	0.320
Wealth index	(Poor)				
	Medium	-0.189	0.127	0.828[0.613,1.117]	0.217
	Rich	-0.012	0.147	0.988[0.738, 1.323]	0.937
Mother Education level	(No education)				
	Primary	0.127	0.151	1.136[.874, 1.475]	0.340
	Secondary & Higher	0.249	0.363	1.283[.736, .2.235]	0.379
Place of residence	(Urban)				
	Rural		0.376	1.699 [1.101, 2.620]	0.017
Preceding Birth Interval	(below 24)				
	24-48	-0.532	0.061	.587 [.479, .721]	0.000
	48+	-0.401	0.099	.669 [.500, .896]	0.000
Fraility (Region)	X^2=8.71				0.000
Var(U)=$\boldsymbol{\theta}$		0.145	0.116		

(# categories shows in bracket as reference)

have considered regional frailty; there were 11 regions in Ethiopia. The variance of the frailty term (Regional frailty) θ=0.145 P-value<0.05, which is significantly different from zero, thus we have enough evidence for the existence of unobserved heterogeneity at regional level. The result indicates that there exists significant heterogeneity of death in the children in terms of their region, even though each children share the same value of the covariate. This implies that there are other factors affecting under-five child mortality at regional level that are not described by the observed variables included in the model (Table 4).

The proportional hazard assumption test for both models was checked using Schoenfeld residuals. As we can see from (Table 5) that both models are satisfying the proportional hazard assumption.

The Table 6 presents the AIC and BIC values of the Cox proportional hazard and semi parametric gamma frailty models. The AIC and BIC values of semi parametric gamma frailty model is found to be minimum as compared to the Cox proportional hazard model, indicating that it is the most efficient model to describe the under-five children dataset.

TABLE 5: Schoenfeld Residuals test for proportionality assumption of Cox Proportional Hazard and Semi-parametric Gamma Frailty Models.

Variables		Cox proportional hazard			Semi-parametric frailty		
		(rho)	Chi-square	P-value	(rho)	Chi-square	P-value
Father Education level	(No education)						
	Primary	-0.07905	2.91	0.0879	-0.08270	3.26	0.07123
	Secondary & Higher	0.04566	0.92	0.3386	0.04593	0.93	0.3354
Type of Birth	(Single)						
	Multiple	-0.07138	2.49	0.1143	-0.06281	1.95	0.1623
Sex of a child	(Male)						
	Female	-0.01849	0.16	0.6904	-0.01897	0.17	0.6829
Source of drinking water	(Piped)						
	Borehole	0.02616	0.31	0.5772	0.03077	0.43	0.5100
	Well	-0.00554	0.01	0.9072	-0.00674	0.02	0.8871
	Surface/Rain/Pond/ Lake	0.03435	0.54	0.4644	0.03711	0.63	0.4275
	Others	0.03622	0.62	0.4321	0.03382	0.54	0.4633
Toilet facility	(Flush)						
	Pit latrine	-0.03759	0.69	0.4068	-0.03809	0.71	0.4004
	Others	-0.04356	0.94	0.3333	-0.04489	1.00	0.3183
Birth order	(1-2)						
	3-4	-0.02107	0.21	0.6477	-0.00004	0.00	0.9992
	5+	0.05850	1.62	0.2027	0.05703	2.82	0.0932
Age at first birth	(<=18)						
	>18	0.01750	0.15	0.7021	0.03450	0.74	0.3900
Wealth index	(Poor)						
	Medium	0.06372	1.93	0.1642	0.05999	1.73	0.1881
	Rich	-0.04567	0.95	0.3293	-0.04223	0.82	0.3643
Mother Education level	(No education)						
	Primary	-0.00035	0.00	0.9939	-0.00357	0.01	0.9377
	Secondary & Higher	-0.00801	0.03	0.8563	-0.00385	0.01	0.9314
Place of residence	(Urban)						
	Rural	-0.02793	0.39	0.5338	-0.02582	0.33	0.5683
Preceding Birth Interval	(below 24)						
	24-48	-0.08065	3.11	0.0779	-0.07751	2.96	0.0852
	48+	-0.08147	2.90	0.0884	-0.06631	2.18	0.1403
Global		NA	23.27	0.2758	NA	24.28	0.2302

TABLE 6: AIC and BIC of Cox Proportional Hazard and Semi-parametric Gamma Frailty Models.

Models	AIC	BIC
Cox proportional hazard	7164.07	7303.48
Semi-parametric Gamma Frailty	7155.36	7294.77

DISCUSSION

The study assessed survival of under-five children and examined the social demographic, social economic, environmental and proximate or biological determinants of under-five mortality in Ethiopia by using Cox proportional hazard and semi parametric shared gamma frailty models by considering region as a cluster. From the Log-rank test there was a significant variation in the failure time (occurrence of death) of different categories of under-five mortality, the father educational level, birth order, age at first birth and mother educational level.

By applying the stepwise selection of variables for both models we obtained: Mothers education level, Type of Birth, Sex of the child, Type of place of residence, Wealth index, Birth order number, Source of drinking water, Age at first birth, Type of toilet facility, Fathers education level, preceding birth interval included in the final analysis of the two models. The findings of our study are similar and consistent to many previous literatures. Several studies also identified birth type to be related with child death as multiple births is associated with a higher risk of child mortality, Preceding birth interval consistent with the studies done by, birth order consistent to the studies done by, place of residence to the studies done by, sex of a child consistent to the study done by were the most determinant and statistically significant for mortality of under five in both Cox proportional hazard and semi parametric frailty models *(Seckin N. Determinants of infant mortality in Turkey. MA Thesis. Ankara: Middle East Technical University; 2009. p.82)*.[5,19-21] These significant were statistically associated with time to death of under-five mortality in Ethiopia. These finding is corroborated with the studies done by *(Seckin N. Determinants of infant mortality in Turkey. MA Thesis. Ankara: Middle East Technical University; 2009. p.82)*.[5,19,22]

Based on the values of AIC and BIC criteria semi parametric gamma frailty model was the most efficient model to describe the under-five children dataset, it is consistent with the study done by *(Seckin N. Determinants of infant mortality in Turkey. MA Thesis. Ankara: Middle East Technical University; 2009. p.82)*. [19,23,24] There was frailty effect (θ=0.145, P-value=0.0000, α=0.05) implied that there exists significant heterogeneity of death in the children in terms of their region, even though each child share the same value of the covariate.[25]

CONCLUSION

In conclusion, we have identified social demographic, social economic, environmental and proximate or biological determinants of under-five mortality in Ethiopia based on recent 2016 EDHS data. The results of both models showed that there are wide range of potential viz., type of birth, birth order, place of residence, sex of a child and preceding Birth interval significantly associated with the under-five child mortality. Therefore, the implication of our findings might be prudent on the part of policy maker to focus on these important factors and also adopt an integrated approach to reduce the under-five child mortality in Ethiopia.

Semi parametric Gamma shared frailty is found to be the best model for under-five children. The model also reflected there is strong evidence of high degree of heterogeneity in the under-five children death. Therefore shared frailty model is an appropriate approach for analyzing the under-five data set than Cox proportional hazard model.

Ethics Approval And Consent To Participate

The ethical clearance for the survey was approved by Ethical Review Board of Central Statistical Agency (CSA), Ethiopia and all participants who agreed to take part in the survey signed a consent form.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

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