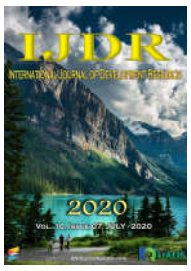
ISSN: 2230-9926

Available online at http://www.journalijdr.com

IJDR

International Journal of Development Research
Vol. 10, Issue, 07, pp. 38357-38367, July, 2020
https://doi.org/10.37118/ijdr.19251.07.2020



RESEARCH ARTICLE OPEN ACCESS

PERFIL EPIDEMIOLÓGICO E SINAIS E SINTOMAS DE IDOSOS COM DOENÇAS REUMATOLÓGICAS: UMA REVISÃO INTEGRATIVA

***Solomon Abebaw**

MSc in Biostatistics, Department of Statistics, Mizan TepiUniversity, Ethiopia

ARTICLE INFO

Article History:
Received 29th April, 2020
Received in revised form
26th May, 2020
Accepted 09th June, 2020
Published online 30th July, 2020

Key words:

Bayesian Analysis, Deviance Information Criteria (DIC), Infant survival, Proportional Hazard models, Random effect models.

****Corresponding author:***
Solomon Abebaw

ABSTRACT

É fundamental compreender o perfil epidemiológico e os principais sinais e sintomas de idosos com doenças reumatológicas visando embasar o desenvolvimento de ações de saúde e, assim, evitar as consequências destas doenças e o impacto sobre a funcionalidade. Neste sentido, este estudo buscou revisar a literatura científica a respeito do perfil epidemiológico e prevalência de sinais e sintomas em idosos com doenças reumatológicas. A metodologia empregada consiste em uma revisão integrativa nas seguintes bases de dados: plataforma digital Biblioteca Virtual em Saúde e Google Acadêmico. Foram aplicados descritores na pesquisa "doenças reumáticas"; "idoso"; "sinais e sintomas". Os critérios de inclusão foram artigos publicados no período de 2010 a 2020, em línguas português, inglês e espanhol, disponíveis na íntegra. Não foram considerados os artigos que não tem como tema central sinais e/ou sintomas de doenças reumatológicas em idosos. Ao todo foram selecionados 08 artigos para a pesquisa. Os resultados indicam que há uma prevalência de doenças reumatológicas em mulheres, com faixa etária de 72,4 anos em média, estes pacientes se queixam de dor e tem doenças associadas como hipertensão arterial sistêmica (HAS) e diabetes *mellitus*. A enfermidade leva a limitação de atividades no cotidiano, privando a autonomia do idoso.

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Citation: ***Solomon Abebaw.*** "Perfil epidemiológico e sinais e sintomas de idosos com doenças reumatológicas: uma revisão integrativa*", International Journal of Development Research*, 10, 07, 38357-38367.

INTRODUCTION

Infant mortality rate (IMR) is one of the most important sensitive indicators of the socioeconomic and health status of a community. More than any other age group of a population, infant's survival depends on the socioeconomic conditions of their environment. Infant mortality is a factor that can be associated with the well-being of a population and taken as one of the development indicators of health and socioeconomic status and also indicates a life quality of a given population, as measured by life expectancy. Infant mortality is also an important demographic, health and development issue for a number of reasons. It is a critical element in the calculation of overall mortality since the highest risk of death and proportion of deaths occur during childhood. It is one of the three measures (along with fertility and migration) that determine population size and growth rate, the age-sex distribution and the spatial spread of the population (Madise *et al.*, 2003).According to the Population Reference Bureau's estimate, globally, in 2012, an average of 41 children per 1000 live births died before reaching their first birthday (age of one). Most infant deaths occur in the less developed world (with 45 infant deaths per 1000 live births in the less developed world compared with 5 infant deaths per 1000 live births in more developed countries. The main reason for the limited progress in reducing infant mortality at the global level, despite more than half the regions having already achieved reductions of more than 50%, is the large and growing share of child deaths that occur in sub-Saharan Africa and South Asia. All 36 countries with child mortality rates above 100 per 1000 births are in sub-Saharan Africa, except for Afghanistan and Myanmar (UNICEF, 2012). Ethiopia is among one of the twenty high-mortality countries but have reduced their under-five mortality rates by more than half since 1990 (UNICEF, 2012). However, much needs to be done to achieve more since with the current figure, one in every 17 Ethiopian children dies before the first birthday (CSA, 2012).Hence, it is important to understand in detail the determinants of infant mortality and knowledge of these factors received great attention by researcher, demographers and biometricians.

Analysis of time to event data, commonly known as Survival Data Analysis, deals with failure time as the dependent variable representing duration until the occurrence of a well-defined event such as death Klein and Moeschberger (2005).

Modeling clustered time-to-event data: Clustered data arises from many applications, for instance in clinical trials where patients are often treated in groups in given hospital centers or countries. The key feature of clustered data is that outcomes from the same cluster are likely to be positively correlated. The proper analysis of clustered data requires that this correlation be taken into consideration. Ignorance of such correlation can bias the statistical inference Ying and Liu (2006). Survival model is widely used in medical field and biostatistics, which can be used to identify the risk factors of an event including the effect of frailty term and can handle the situation when risk factors change with time.Often the timing of an event depends on the location (spatial). There are two approaches to capture the spatial factors in spatially correlated survival data, namely geostatistic approach using geographic location (latitude and longitude) and lattice approach which uses position of a region or location relative to another. Developed a hierarchal spatial survival models involving Conditional Autoregressive (CAR) distributed random effects (frailty). Inclusion of random effects or frailty term in the model can be used to address specific cases (for instance the case with spatial data) where there is diversity or variance sources that can't be explained by a vector covariate in the model(Banerjee, S., Wall, M. M., & Carlin, 2003).

Objective of the study

General objective: The main objective of the study was to explain the pattern of infant mortality differentials across population subgroups while accounting for possible (spatially correlated) differences in hazard among the regions.

Specific objectives

- To identify potential risk factors associated in infant mortality while accounting for possible differences in hazard among the regions.
- To provide information based on the result of the study to police makers and researchers in the area.

Significance of the Study: It contributes to a comprehensive and better understanding of factors behind the increase of infant mortality in the country. To provide information and evidence for pertinent and stakeholders, such as Governmental, non-governmental organizations and other partners in the health sector to know and understand the important areas they need to focus on to develop policies,programmers and projects to reduce infant mortality rates.

DATA AND METHODOLOGY

EDHS 2016 data

The 2016 Ethiopia Demographic and Health Survey (2016 EDHS) is part of the worldwide MEASURE DHS project which is funded by the United States Agency for International Development (USAID). The survey was conducted by the Central Statistical Agency (CSA) under the auspices of the Ministry of Health. .

Infant mortality data: Information on infant mortality data was found from the birth history of women who were included in the survey. The interest of this study was about infants from birth until the age of one year, which includes 4057 children's information.

The response and covariates: The response /outcome variable for this study was the survival time of infants measured in months from birth until date of death or censored (if infants survive past 12 months).

Predictors: The main covariates were used in this study and the code of categories are described in the below table.

Table 1. Variables and their descriptions

covariates/factors	Definition, Categorization and Codes
Child's sex	Sex of infant (1= Male; 2= Female)
Residence	Place of residence for infants' (1=Rural; 2=Urban)
Mother's education	Mother's level of education coded as (0= No education; 1= Primary; 2= Secondary and above)
Mother's age	The age of the mother's at the time of the most recent birth. Coding is done in three cohorts: (0 <20 year ;1 =20 - 29 years ; 2 >= 30 years
Father's education	Father's level of education (0= No education; 1= Primary; 2= Secondary and above)
Birth order	birth order of infants (0= 1st birth ; 1= 2nd – 5th birth ; 2=6th and above birth)
Birth interval	The length of time between two successive live births (1 < 24 months, 2>= 24 months)
Type of birth	0 = Single birth (if infant was born singly) 1 = Multiple (if infant was born in multiple of two, three ….)
Breast feeding Status	Breastfeeding status of infants from the respondent (0= No Breast feeding; 1= Breast feeding)
Wealth index	Household wealth index that measures the standard of living of the family that the child belongs, based on characteristics related to the socio-economic status of a household. (1= Poor; 2=Medium; 3=Rich)
household size	Total number of household members or number of family (0=1-4 number of family; 1=5- 8 number of family ; 2= 9 and above number of family
Source of water	The source of drinking water classified as (0 = Protected ; 1 = Unprotected)

Survival analysis: The term survival analysis pertains to a statistical approach designed to take into account the amount of time an experimental unit contributes to a study. The purpose of survival analysis is to model the underlying distribution of the failure time variable and to assess the dependence of the failure time variable on covariates. Survival data are different from other types of continuous data because throughout study the endpoint of interest is not necessarily observed in all subjects. This may occur because:

- Some patients are lost to follow-up, that is, they are not followed to the end of the study and, when last seen, have not experienced the event of interest, or
- The event has not occurred in some patients by the time the study ends for analysis. Such data are referred to as censored survival times and are different from missing data in that they provide a lower bound for the actual non-observed survival times.

The Kaplan-Meier (Product Limit Method) Estimator: Suppose there are n observations, $t_1, t_2, \dots\dots, t_n$ with corresponding censoring indicators,$\delta_1, \delta_2, \dots\dots, \delta_n$. Let the number of distinct event times be r (r ≤ n), with the ordered event times given by $t_{(1)} \leq t_{(2)} \leq \dots\dots \leq t_{(r)}$and corresponding number of events $d_{(1)},\dots, d_{(r)}$. And also let $R(t_{(j)})$denote the risk set at the event time $t_{(j)}$, i.e., the set of subjects that did not yet experience the event and were not yet censored before time $t_{(j)}$and thus still at risk for the event atthat time. Therefore, the Kaplan-Meier estimate of the survival function (Kaplan and Meier, 1958) at time t is givenby:

$$\hat{S}(t) = \prod_{j=1}^{k} \frac{R(t_{(j)}) - d_{(j)}}{R(t_{(j)})} \text{ , for } t_{(j)} < t \leq t_{(j+1)} \text{ , } k = 1,2,$$

Parametric proportional hazards model: The parametric proportional hazards model is the parametric versions of the Cox proportional hazards model. The key difference between the two kinds of models is that the baseline hazard function assumed to follow a specific distribution when a fully parametric PH model fitted to the data, whereas the Cox model has no such constraint.Hazard ratios have the same interpretation and proportionality of hazards still assumed.

Weibull Proportional Hazard Model: The Weibull PHis one of the parametric distributions, which are used for the analysis of life time data and mostly used in literature for modeling life time data. Weibull PH model is more general and flexible than the other parametric proportional distribution and allows for hazard rates that are non-constant but monotonic.(Ibrahim *et al*., 2001 and Yu, 2006). Under the WeibullPH model the hazard function of a particular individual with covariatesis given by,(Klein and Moeschberger, 2005)

$h(t/X) = \rho {t_{ij}}^{\rho-1} \exp(\beta_1 x_1 + \beta_2 x_2 + \dots + \beta_p x_p) = \rho {t_{ij}}^{\rho-1} \exp(\beta' X)$Where ρ is a shape parameter for the baseline hazard of Weibull distribution with ρ>1 reflecting a monotonically rising hazard rate, ρ<1 reflecting a monotonically declining hazard, and ρ =1 reflecting a flat hazard,$X = (x_1, x_2, \dots, x_p)^t$is the values of the vector of explanatory variables for a particular individual, and $\beta' = (\beta_1, \beta_2, \dots, \beta_p)$ is a vector of regression coefficients.

Standard frailty models: A frailty model is a generalization of a survival regression model. In addition to the included covariates in the survival model, a frailty model also accounts for the presence of a latent multiplicative effect on the hazard function. This effect, or frailty, is not directly estimated from the data, but instead is assumed to have unit mean and finite variance, which is estimated (Gutierrez, 2002).

For subject (infant) j ,j= 1, 2, ... , n_i,from cluster (region) i, where i =1, 2, ... , I, we observe X_{ij} ,the minimum of the censoring timeC_{ij} and t_{ij} is the time to death for subject j in region iand the censoring indicator δ_{ij} = I($t_{ij} \leq C_{ij}$).The ${t_{ij}}'s$ and C_{ij}'s are assumed to be independent.The shared frailty model is defined as (Hougaard, 2000).

$$h(t_{ij}, X_{ij}) = h_{0i}(t_{ij})\, u_i \exp(\beta^T X_{ij}) = h_{0i}(t_{ij}) \exp(\beta^T X_{ij} + w_i)$$

Wherei indicates thei^{th} cluster and j indicates thej^{th} individual for the i^{th} cluster, $h_{0i}$is the baseline hazard function, $w_i = \log u_i$is the region-specific frailty term designed to capture differences among the strata /the random term of all the subjects in cluster i.Typically a simple $i.i.d$ specification for w_i is assumed.X_{ij} the vector of covariates for subject j in cluster i, and β the vector of regression coefficients. If the number of subjects is 1 for all groups, the univariate frailty model is obtained (Wienke, 2010); otherwise the model is called the shared frailty model (Therneau and Grambsch 2000).

Weibull PH models with gamma frailty: The study is intended to focus on the parametric PHmodels with gamma frailty under the shared frailty part, results of model fit are compared to those from the parametric fit, in particular the weibull, which is the most commonly, used distribution on the baseline and itshazard is given as: (Hougaard, 2000).

$$h(t_{ij}, X_{ij}) = \rho {t_{ij}}^{\rho-1} \exp(\beta^T X_{ij} + w_i)$$

In cases where the expected values of frailtyis greater than one, subjects experience an increased hazard (or risk) of failure and are said to be more frail than their cohorts. In this way, frailty models can provide a useful alternative to a standard survival model when the standard model fails to adequately account for all the variability in the observed failure times. In shared frailty models, independent random effect was assumed; infact it is not always valid. In this study, because of a mathematically convenient choice for the distribution of w_i (random effect) the study used gamma distributions, as a single heterogeneity parameter (denoted by θ) given by

$$f(w) = \frac{\theta^{\frac{-1}{\theta}} w^{\frac{1}{\theta}-1} \exp(-w/\theta)}{\Gamma(1/\theta)}, \theta > 0$$

Where and $E(w) = 1$ and $var(w) = \theta$, the parameter θ provides information on the variability (the heterogeneity) in the population of clusters i.e small value of $1/\theta$reflect a greater degree of heterogeneity among groups (clusters) and a stronger association within groups.

Spatial frailty model: Spatial frailty model is an extension of the ordinary frailty models by allowing random effects accommodating spatial correlations to enter into hazard function multiplicatively. According to Li and Ryan (2002), a spatial frailty model is formulated as follows. In each of I geographic regions , a number of subjects, say, n_i (i = 1,.., I), are followed until the event happened or censoring, whichever comes first. For each individual, along with the observed censored time $Y_{ij} =$ min (T_{ij}, C_{ij}) and non-censoring indicator $\delta_{ij} = I(T_{ij} \leq C_{ij})$, where T_{ij} and C_{ij} are underlying true survival and censoring time, respectively, a length-p covariate vector $x_{ij}$are also observed. Here I(.) is an indicator function. We assume that the censoring times C_{ij} are independently distributed and are independent of the T_{ij}, given the observed covariates, and that the distributions of C_{ij} do not involve in the parameters of interest. The Weibull proportionalhazard model with spatially correlated frailty is given as

$$h(t_{ij}, X_{ij}) = \rho t_{ij}^{\rho-1} \exp(\beta^T X_{ij} + w_i)$$

Where w_i represents the i[th] partition areas of region D indexed in a discrete pattern. Partitions are referred to as the 'lattice/ regions'. This model uses the method combining information about the areas adjacent to each other/its neighbor's compared to metric distance information. As a result, the distribution of random effect W is defined as,W|λ~ CAR(λ), and are called as conditionally autoregressive model which indicates the existence of spatial dependence on the composition of covariance, where λ is the CAR parameter distribution stating precision or variance of its random effect distribution.

Likelihood of Bayesian Survival Model: Suppose$t = t_{ij}, x = x_{ij}, w = w_i, and \delta = \delta_{ij}$, where δ_{ij} is a death indicator for all subject in all clusters (1 if child is died before one year, 0 if censored/survived) are the notations.Then for the weibull parametric PHmodel, the joint posterior distribution is given by:

$$p(\beta, w, \rho, \lambda/t, x, \delta) = L(\beta, w, \rho, t, x, \delta) p(w/\lambda) p(\rho) p(\beta)\, p(\lambda)$$

Where $p(w/\lambda)$ is the CAR distribution of the frailty, $p(\beta)$ and $p(\lambda)$ are the prior and hyper prior distribution on,β and λ respectively, $p(\rho)$is also prior for baselineρ and $L(\beta, w, \rho, t, x, \delta)$ is the likelihood for the Weibull model with spatial shared frailties proportional to:

$$L(\beta, w, \rho, t, x, \delta) = \prod_{i=1}^{I} \prod_{j=1}^{ni} \{\rho t_{ij}^{\rho-1} exp(\beta^T x_{ij} + w_i)\}^{\delta_{ij}} exp\{-t_{ij}^{\rho} exp(\beta^T x_{ij} + w_i)\} \quad (1)$$

Here including both shared spatial and non-spatial frailties is certainly possible in lattice modeling; the likelihood for this becomes:

$$L(\beta, w, \rho, t, x, \delta) \propto \prod_{i=1}^{I} \prod_{j=1}^{ni} \{\rho t_{ij}^{\rho-1} exp(\beta^T x_{ij} + w_i)\}^{\delta_{ij}} exp\{-t_{ij}^{\rho} exp(\beta^T x_{ij} + w_i + V_i)\}$$

Where V_i is non spatial frailty term ($V_i \sim N(0, 1/\tau)$),w_i have conditional autoregressive prior ($W|\lambda \sim$ CAR (λ)) and the rest of the notations remains as it is above (1).

Bayesian Model Selection: The simple and intuitively appealing extension of the AIC criterion called the deviance information criterion, DIC (Spiegelhalter *et al.,*2002), is based on the posterior distribution of the deviance statistic as,

$$D(\theta) = -2 log f(y|\theta) + 2\, log h(y)$$

Where $f(y|\theta)$is the likelihood function for the observed data vector y given the parameter vector θ and h(y)is some standardizing function of the data alone (which thus has no impact on model selection). In this approach, the fit of a model is summarized by the posterior expectation of the deviance,$\overline{D} = E\{\theta/y(D)\}$, while the complexity of a model is captured by the effective number of parameters, pD. It is show that a reasonable definition of pD is as follows (Spiegelhalter *et al.,* 2002).

$$pD = \mathrm{E}\theta|y\ [D] - D(\mathrm{E}\theta|y\ [\theta]) = \bar{\mathrm{D}} - D(\bar{\theta})$$

i.e the expected deviance minus the deviance evaluated at the posterior expectations. The DIC is then defined analogously to the AIC as the expected deviance plus the effective number of parameters, i.e.

$$DIC = \bar{\mathrm{D}} + pD$$

Since small values of $\bar{D}$ indicate good fit while small values of pD indicate a parsimonious model, small values of the sum (DIC) indicate preferred models.

RESULT AND DISCUSSION

Exploratory Analysis: The major demographic and socio-economic characteristics of the respondents with infant mortality are presented in Table 2 below. The total number of children covered in the present study was in 4057. Among these, 2093(51.58 %) were male infants whereas 1964(48.42%) were female infants. A high proportion of death was observed among male infants 19.6% as compared to female infants 16.7 %. Table 2 also shows, a total of 3377 (83.24%) and 680(16.76 %) of infants were born from the rural and urban part of Ethiopia respectively.

Table 2. Frequency and Percentage for Baseline Covariates with the Observed number of Infant Mortality status in Ethiopia

Covariates	Categories	censored	dead (%)	Total (%)
Place of residence	Rural	2735	642(19.0)	3377(83.24)
Urban	582	98(14.4)	680(16.76)	
Mother education	No education	2236	529(19.1)	2765(68.15)
Primary	878	187(17.6)	1065(26.25)	
Secondary+	203	24 (10.6)	227(5.60)	
Father education	No education	1640	414 (20.2)	2054(50.63)
	Primary	1241	252(16.9)	1494(36.83)
	Secondary+	436	73(14.4)	509(12.54)
Breast feeding	yes 2920	472 (13.9)	3392(83.61)	
No397	268 (40.3)	665(16.39)		
Mother's age	<20 216	74 (26.4)	280(6.90)	
20-29	1832	350 (16.0)	2182(53.78)	
>=30	1279	316 (19.8)	1595(39.32)	
Birth order	first 579	153(20.9)	732(18.04)	
	2 – 5	1871	390 (17.2)	2261(55.73)
	6+	867	197(18.5)	1064(26.23)
Child's sex	male 1682	411 (19.6)	2093(51.58)	
	Female 1635	329 (16.7)	1964(48.42)	
Type of birth	Single	3208	667(17.2)	3875(95.51)
Multiple109	73(40.1)	182(4.49)		
Birth interval	<24 months1184	337(22.2)	1521(37.49)	
>=24 months2133	403(15.9)	2536(62.51)		
Family size	1 – 4933	275 (22.8)	1208(29.78)	
	5 – 81943	389(16.7)	2332(57.48)	
	9 and more 441	76 (14.7)	517(12.74)	
Wealth index	poor	1624	392(19.4)	2016(49.69)
	Medium	544	124(18.5)	668 (16.47)
Rich	1149	224(16.3)	1373(33.84)	
Source of water	protected	2133	457 (17.6)	2590(63.84)
Unprotected	1184	283(19.3)	1467(36.16)	

Table 3. Posterior summary for non-frailty effect model

Covariates	Node	Estimate	SD	Mc error	2.5%	97.5%	
Constant	beta[0]	-5.1103	1.8140	0.0730	-7.3490	-3.7910	
Place of residence(Rural)	beta[1]	0.1485	0.0815	0.0050	0.0718	0.2970*	
Child sex (female)	beta[2]	-0.0764	0.1044	0.0052	-0.2326	0.0752	
Mother's educatn (primary)	beta3[1]	-0.2531	0.1072	0.0059	-0.4119	-0.1029 *	
Secondary and above	beta3[2]	- 0.4162	0.1362	0.0171	-0.6121	-0.1382 *	
Mother's age (20-29)	beta4[1]	-0.2448	0.1932	0.0239	-0.6498	- 0.1265 *	
>=30	beta4[2]	-0.2817	0.1604	0.0205	-0.6179	-0.1368 *	
Father's education (primary)	beta5[1]	-0.1340	0.0824	0.0038	-0.2031	0.0153	
Secondary and above	beta5[2]	-0.2226	0.1019	0.0129	-0.3980	0.0282	
Breast feed	beta[6]	-0.4716	0.1151	0.0150	-0.5165	-0.0658 *	
Birth order (first birth)	beta7[1]	0.2352	0.2246	0.0211	0.0291	0.5130 *	
2-5 order	beta7[2]	-0.0163	0.0854	0.0104	-0.1370	0.2081	
Family size (5- 8 members)	beta8[1]	0.0406	0.0784	0.0067	-0.1159	0.1989	
>=9 members	beta8[2]	0.1224	0.0981	0.0098	-0.0529	0.2901	
Type of birth (multiple)	beta[9]	- 0.0853	0.1603	0.0142	-0.1930	0.2824	
Wealth index (medium)	beta10[1]	0.0866	0.0890	0.0108	-0.2062	0.2147	
Rich	beta10[2]	-0.0710	0.1710	0.0135	-0.2903	0.1552	
Source of water (un protected)	beta[11]	0.1726	0.0308	0.0037	0.1027	0.3048*	
Birth interval (< 24 months)	beta[12]	0.3119	0.0522	0.0035	0.2851	0.4129*	
ρ	0.7973	0.0236	0.0015	0.7522	0.8455*		
PD = 19.74	DIC = 5296.62						

Table 4. Posterior summaries for the non-spatialshared frailty

Covariates	Node	Estimate	SD	Mc error	2.5%	97.5%
Constant	beta[0]	-2.8787	2.4042	0.1497	-5.6500	-0.3770
Place of residence(Rural)	beta[1]	0.1545	0.0771	0.0028	0.0515	0.2543 *
Child sex (female)	beta[2]	-0.0344	0.0874	0.0041	-0.1857	0.1166
Mother's educatn (primary)	beta3[1]	-0.2261	0.0960	0.0047	-0.3526	-0.0647*
Secondary and above	beta3[2]	-0.3750	0.2278	0.0177	-0.5834	-0.0729*
Mother's age (20-29)	beta4[1]	-0.2192	0.1913	0.0130	-0.5621	-0.0876*
>=30	beta4[2]	-0.1856	0.1047	0.0049	-0.4595	-0.0959*
Father's education (primary)	beta5[1]	-0.0340	0.0792	0.0031	-0.1730	0.0453
Secondary and above	beta5[2]	-0.1812	0.1612	0.0105	-0.3861	0.0476
Breast feed	beta[6]	-0.4252	0.2426	0.0170	-0.5993	-0.0786*
Birth order (first birth)	beta7[1]	0.2421	0.1983	0.0109	0.0173	0.4602*
2-5 order	beta7[2]	-0.0803	0.0139	0.0017	-0.2723	-0.0479*
Family size (5- 8 members)	beta8[1]	0.1274	0.1045	0.0056	-0.0424	0.2909
>=9 members	beta8[2]	0.1406	0.0960	0.0035	0.0132	0.3381*
Type of birth (multiple)	beta[9]	0.0985	0.2417	0.0207	-0.2011	0.2863
Wealth index (medium)	beta10[1]	-0.0836	0.2019	0.0132	-0.3060	0.1338
Rich	beta10[2]	-0.0935	0.1064	0.0105	-0.2986	0.1106
Source of water (unprotected)	beta[11]	0.3126	0.0954	0.0043	0.1139	0.4294*
Birth interval (24 < months)	beta[12]	0.4019	0.0775	0.0019	0.3051	0.4829*
ρ	0.8796	0.0247	0.0008	0.8321	0.9280*	
θ	0.4072	0.1251	0.0248	0.0523	0.7640*	
PD = 29.19	DIC = 5172.70					

Table 5. Posterior estimate summaries for the spatial shared frailty model (CRA frailty)

Covariates	Node	Estimate	SD	Mc error	2.5 %	97.5 %
Constant	beta[0]	-2.97821	2.2108	0.1330	-5.2401	-0.3736
Place of residence(Rural)	beta[1]	0.1547	0.0588	0.0026	0.0532	0.2139*
Child sex (female)	beta[2]	-0.0354	0.0742	0.0035	-0.1767	0.1048
Mother's educatn (primary)	beta3[1]	-0.2354	0.0781	0.0039	-0.3135	-0.0539*
Secondary and above	beta3[2]	-0.3754	0.1471	0.0103	-0.4310	-0.0813*
Mother's age (20-29)	beta4[1]	-0.2261	0.0908	0.0030	-0.3011	-0.0978*
>=30	beta4[2]	-0.1837	0.0870	0.0028	-0.2881	-0.0962*
Father's education (primary)	beta5[1]	-0.0342	0.0522	0.0023	-0.1312	0.0431
Secondary and above	beta5[2]	-0.1831	0.1119	0.0065	-0.3374	0.0154
Breast feed	beta[6]	-0.4273	0.0918	0.0032	-0.4816	-0.1091*
Birth order (first birth)	beta7[1]	0.2433	0.1975	0.0106	0.0169	0.4721*
2-5 order	beta7[2]	-0.0998	0.0136	0.0012	-0.2683	-0.0237*
Family size (5- 8 members)	beta8[1]	0.1281	0.0964	0.0042	-0.0406	0.2714
>=9 members	beta8[2]	0.1451	0.1071	0.0063	-0.0413	0.3021
Type of birth (multiple)	beta[9]	0.0961	0.2106	0.0160	-0.1910	0.2175
Wealth index (medium)	beta10[1]	-0.0156	0.1564	0.0079	-0.2645	0.1338
Rich	beta10[2]	-0.0941	0.1045	0.0058	-0.2536	0.1504
Source of water (unprotected)	beta[11]	0.3218	0.0926	0.0031	0.2207	0.4162*
Birth interval (< 24 months)	beta[12]	0.4215	0.0751	0.0017	0.3651	0.4674*
ρ	0.8947	0.0244	0.0007	0.8432	0.9286*	
λ	0.7561	0.1476	0.1062	0.2641	0.9783*	
PD = 27.02	DIC = 5128.33					

The proportions of infant death under based on the two residences were 19.0% and 14.4% respectively. With regard to educational attainment, 2765 (68.15%) mothers and 2054(50.63%) fathers had no education while 1065(26.25%) mothers and 1494(36.83%) fathers had primary education and the remaining 227(5.60%) mothers and 436 (14.4%) fathers had a secondary and above level of education. A high proportion of infant death observed in non-educated parents. A total of 740 (18.24%) infant died within 12 months after birth, this is a very high level of infant mortality. Most of the death occurred in the early months after births and then the rate decline as the age of the infant got closer to twelve months. The Kaplan-Meier estimator was applied to estimate the survival curves for selected covariates. The plot of the Kaplan-Meier estimates for the wholeinfant data and for selected categorical covariates; Place of Residence, Sex of Infants and Mothers' Education level are displayed in Figure1 below. From the plot,we can see that the estimated survival function curve for urban area is above that of ruralarea over the entire follow up period, giving evidence for a higher probability of survival and lower risk of death for an urban as compared with the rural. The survival function of a female infantis greater than a male infant. This indicated thatfemale infants have better survival time than male infants.The plot also shows there was a significantdifference in education level mothers. Infants born from better-educated mothers have a better survival rate.However, making a decision based on graphical outputs might be subject to personal bias, so we undertake a more formal test based on non-parametric methods.

Multivariable Weibull Modeling: We also summarized the results for the standard survival analysis that ignores any frailty variation across the region in Table 3, followed by including frailty variation across region in Table 4 and spatial shared frailty variation in Table 5. Simulation summaries (estimate, standard errors, Mc errors and 95% Bayesian credibility interval limit formed by taking the 2.5 and 97.5 posterior percentiles) for the expected predictors of survival or time to death of infants are considered as the final output for the evaluation of the modelling strategy.

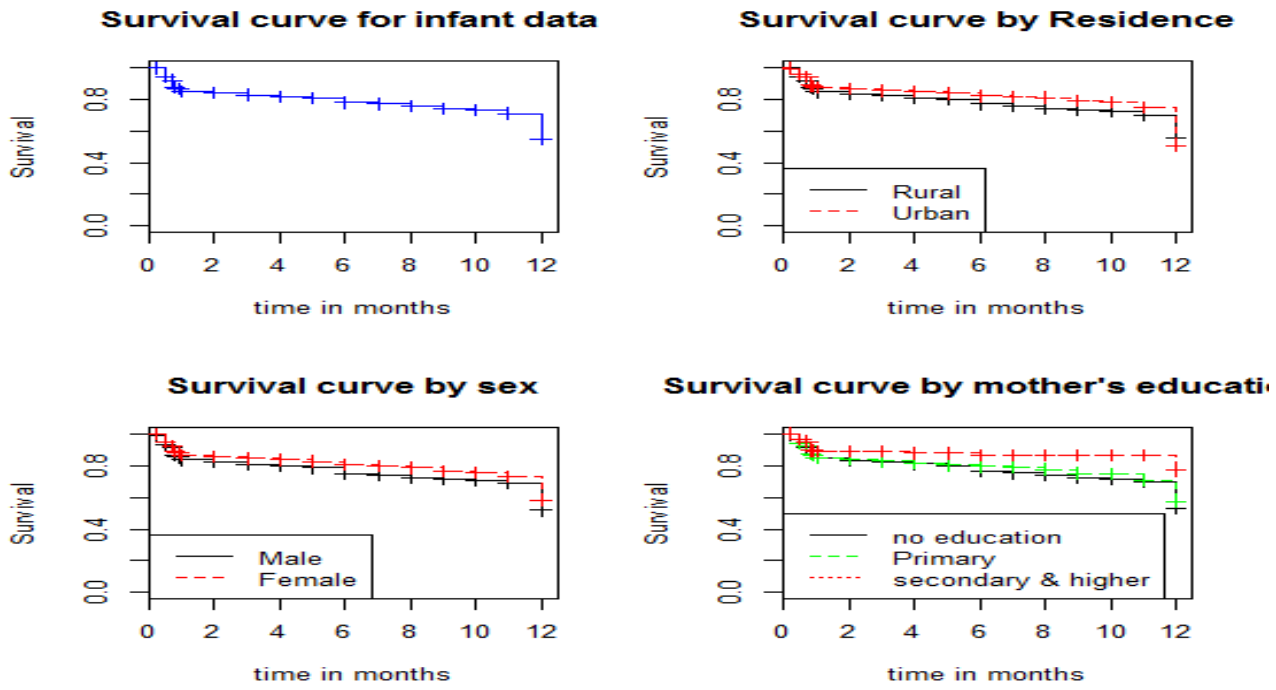

Figure 1. Kaplan-Meier estimates of the Survival Curves

To evaluate the precision of the parameter estimate also, one should keep an eye on the sd (standard error) and MC error under node statistics. The standard deviation of the estimated statistic (called standard error) measures the variability of the posterior estimates while the MC error quantifies the variability in the estimates that is due to Markov chain variability. Table 3, Table 4, and Table 5 all provides posterior estimate summary of non-frailty, non-spatialshared frailty and CAR frailty (spatial) models for the main and random effect in our three frailty models respectively. In all cases of the models, the results are based on three parallel MCMC sampling chains of 50,000 iterations each, following a 25,000 iteration burn-in period with different starting initial values are used to improve the convergences. All the initial values was obtained from the Weibull estimate for parameters. The result shows among the covariates place of residence, maternal education and age at birth, breastfeeding, birth spacing (interval),first birth orders and source of drinking water was found statistically significant at 5% significant level in all models (as the 95% credible interval doesn't include zero). Covariates gender of the child, type of birth, level of father's education, family sizes 5 -8 members and wealth index of household was found statistically insignificant in all three cases. Birth order 2 -5 was also found statistically insignificant in thenon-frailty model but it was significant in both frailty models at 5% significant level. Family size 9 and more members is significant only under non-spatial model but not in other cases.

All the above results also show that the estimate of the shape parameter ρ is quite similar trends across models and its values were significantly less than 1, indicating that a decreasing baseline hazard of death overtime. This is consistent with the fact that a high proportion (471, or 64%) of the infant deaths in my dataset occurred in the first monthof life, the force of mortality (hazard rate) is very high initially, but drops quickly and continues to decrease throughout the first year. As in all table above shown, in each of the three comparisons between the spatial, non-spatial and non-frailty models, the spatialshared frailty random effects (CAR frailty) model outperform the best among the other models, as indicated by the smaller DIC values 5128.33 with PD of 27.02. The model also resulted ina higher unit of difference (44 units) in DIC value than the second best model, indicating substantially superior. This shows there is spatial dependence in the infant mortality that is not fully captured by the substantive covariates in the model. Therefore, we believe that the survival status of an infant affected by geographical regions. Treating the random effects as though they were spatially independent, as we typically do reflects model misspecification. In survival analysis usually, we are interested in hazard rate; hence the exponential of coefficient estimates (the posterior mean) i.e. $e^{beta[i]}$ where i is the number of significant covariates tells us the hazard of infant's to mortality risk (the hazard ratio). So the interpretations of the findings of the study covariates with incorporations of clustering/ regional effects are also provided below according to the selected best model (the CAR frailty model) which considers the random effects between the clusters are correlated.

Place of residence: The reference group here was an urban area. The estimated posterior mean hazard ratio of infants born in a rural area was 1.1672 (95% CI: 1.0546, 1.2385) implying that the risk of death for infants born in a rural area was 16.72% higher than infants born in an urban area (the reference group). The 95% credible interval also indicates that the risk of death for infants born in a rural area is as low as 1.0546 (5.46%) and as high as 1.2385 (23.85 %) times the risk of death for infants born in urban areas. Therefore, the place of residence has a significant influence on the survival probability of infants. Mother's age: the reference group was here the age group less than 20 years. Infants born from mothers of the age group of 20-29 years died at a rate which was about 20.24% lower than those born from mothers in the reference age group (HR= 0.7976, 95% CI:0.7400, 0.9068).For mother's age group 30 and above years the estimated hazard ratio was 0.8322 (95% CI: 0.7497, 0.9082), shows that infants born to mothers of the age of 30 and above years died at the rate which about 16.78 % lower than those born to mother's

age below 20 years. This showed that infants born to mothers of age under 20 years were more likely to experience a very high rate of mortality. Mother's level of education: In this case, the reference group was no education or illiterate mothers. The posterior mean hazard ratio of infants whose mothers had primary level of education was 0.79025 (95% CI: 0.7309,0.9475) and for the secondary and above level, it was 0.6870 (95% CI: 0.6498, 0.9219) showing that infant born to mothers of those educational levels died at rate were 20.98% and 31.30% respectivelylower than infants whose mothers had no education. These results indicated that the risk of infant mortality was decreasing with the increasing of mother's education level and it was also found that mother's education has a significant effect on infant mortality. Breast-feeding*:* the reference group here was mothers who were not breast-fed their child. The estimated posterior mean hazard ratio for infants who were breastfed was 0.6523 (95% CI: 0.6178, 0.8966) showing that infants who were breastfed died at a rate which was about 34.77% lower than infants were who were not breastfed controlling for other covariates in the model. The 95% credible interval suggested that the hazard of death for an infant who was breastfed could be 0.6178 times at minimum and 0.8966 times at maximum lower as compared to those who were not breastfed. Birth order: the reference group here was infants born in the birth order 6 and above. The estimated hazard ratio for firstborn infants and infants in the birth orders 2-5 was 1.2755 (95 % CI: 1.0170, 1.6034) and 0.9050 (95% CI: 0.7647, 0.9765) respectively. The interpretations are that: the firstborn infant had 27.55% higher risk of death than infants belongs to order six and more (reference category), but for infants belongs to birth orders 2-5 the risk was 9.5 % lower than infants in the reference group controlling for other covariates in the model.

This study also indicated that the birth interval is significantly associated with infant mortality. Infants born within an interval of fewer than two years have a higher mortality risk than infants born with an interval of two or more years. In particular, the estimated hazard ratio for infants born in preceding birth interval less than 24 months was 1.5242 (95% CI: 1.4407 , 1.5958) implying that the risk of death for infants born with preceding birth interval less than 24 months was higher by about 52.42% relative to infants born in preceding birth interval 24 months and above (the reference group). This implies that shorter preceding birth intervals were associated with increased infant deaths.

DISCUSSION

The DIC criterion (Spiegelhalter *et al.*, 2002) to appear was used to choose among various competing models. Thus, examining the DICs for the various models, clear patterns emerged. The models that incorporate spatial dependence in region-level frailties are the preferred model. Beside of this aim, this study was also identifies a risk factors of infant mortality in Ethiopia using the nationally representative 2016 EDHS data. Regarding the place of residence or geographical position of households, the study shows that rural areas have a higher rate of IM than the urban areas. The finding is in line with what was found by Kumar and File (2010) in Ethiopia shows that most of the deaths of children occurred in a rural area. A similar study by Tarig and Sideeg (2010) also found that children residing in urban areas have a better chance of survival than those residing in rural areas.This could be due to the fact that urban areas had good infrastructures and better access to health facilities than the rural ones. Mother's education is the most important determinant of infant mortality among the mother's characteristics that are considered in this study. The current study revealed that the risk of infant mortality was decreasing with the increasing of mother's education level and it is also found that mother's education has a significant effect on infant mortality. The finding is in line with what was found by Kabir and Uddin (2012) in urban Bangladesh from the Cox regression model result shows that mother's education level has a significant impact on infants' mortality showing that children born to literate mother have the highest chance of survival. A similar result also obtained in Ethiopia by Kumar and File (2010), in southern Sudan Mahfouz *et al*.,(2009).The possible reason could be mothers with higher education might probably have better access to the utilization of health facilities and higher income helps mothers to have the ability to purchase goods and services that in turn helps to improve infants' health. Furthermore, the findings also showed that those infants whose mother's age is 20 and above years have less likely to experience an infant death compared to infants whose mother age is under 20 years. These findings are consistent with findings from other studies (Balk *et al*., (2004), Girson and Maurice (2010). They found that maternal age at first birth has a significant effect on infant mortality showing that infants born to a very younger mother experienced the highest risk of dying. Another study by Rustein (2008) in developing countries, also found that age of the mother parity and child mortality relationship had a U-shaped pattern; mortality risks were highest among children born to very young mothers and those born to older mothers. The higher risk of dying among infants born to young maternal ages may be as a result of due to physical immaturity, lack of child care skills and access to health care services.

The study also revealed that of the nutritional factors breastfeeding is positively related to infant's survival chances. Infants who were not breastfed died at a higher rate than infants who were breastfed. This result is parallel to the literature on infant mortality. In literature, most of the studies also suggest a positive relation between infant health and breastfeeding (Palloni and Tienda 2004, Murphy and Wang 2008, Mustafa and Odimegwu (2008) in Kenya,Kayode*et al.* (2012) in Nigeria from the result of logistic regression model). The current study revealed that firstborn infants experience a higher risk of dying than infants whose birth order is six and above; infants with birth order two up to five have a lower risk of dying than infants whose birth order is six and above. The finding is consistent with the studies point to U-shape effects of birth order, with the probability of infant mortality declining after the first child and increasing again for children of birth order five and higher (Kombo and Ginneken (2009) in Zimbabwe, Titaley *et al*., 2008 and Uddin and Hossain, 2008). Another study by Desta (2011) in Ethiopia and Balk *et al.,* (2004) in West Africa also they found that birth order is one of the determinants of infant mortality showing that a firstborn infant was exposed to a high risk of mortality. Also among maternal biological factors, birth interval with the previous child has a strong relationship with infant mortality for the index child. The result indicates that the infant mortality rate is found to be the highest for infants having less than two years of a birth interval with the previous child and lowest for the infant whose birth interval was two years and above. This finding has conformed to the other studies that the length of the birth interval is positively correlated with the survival of the infant mortality (Abe and Oladeji, (2013), Omariba *et al.,* 2007) in Kenya, Kayode*et al.,* (2012) in Nigeria).

Short birth interval increases the risk of infant mortality due to physiological and nutritional depletion of the mothers which relate the mothers exposed to a pregnancy complication. The findings of this study also revealed that the risk of infant death was higher for infants born in a household with access to unprotected drinking source of water as compared to those born in a household with access to a protected source of water. The finding is in line with what was found by Samuel (2011) Using data from the 2005 EDHS showed that the risk of death for infants born in households with access to unprotected drinking water is higher by 47% relative to those born in households with access to protected drinking water. In this study, we used the region as a clustering (frailty) effect on infant mortality in Ethiopian using 2016 EDHS data. The spatial clustering effect wassignificant (as 95% CI:0.2641, 0.9783 does not include one) in Weibull spatial shared frailty model. This showed that there was spatial dependency between regions in which neighboring regions share similar risk factors on mortality i.e., the correlation between regions cannot be ignored and clustering effect was important in modelling the hazard function.

List of Abbreviations: Infant mortality rate (IMR), Deviance Information Criterion (DIC), Mizan-Tepi University (MTU), andOdd ratio (OR)

Consent for publication: Not applicable since there is no protective individuals in the participants

Competing Interests: The author declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Authors 'contributions: Solomon Abebaw was responsible for the conception,data analysis, report and in the preparation of the draft manuscript, interpretation and reconsideration of the paper.

Acknowledgments: All who contributed for data extraction and collection are duly acknowledged.

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