



Causes of Discontinuity and Becoming Inactive of Blood Donation among Donors in the National Blood Bank Service, Addis Ababa, Ethiopia: A Retrospective Cohort Study

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Abstract

Background: The demand for blood and blood products is increasing all over the world. Despite the fact that many people are eligible to donate, the number of people who donate on a regular basis within the recommended time frame is also very small. This study aimed to assess the determinant factors of time to return of voluntary blood donors at the National Blood Bank Service, Addis Ababa, Ethiopia.

Methods: A retrospective cohort study was conducted on all volunteer blood donors who donated blood from 06 September 2017 to 11 September 2018 at the National Blood Bank Service, Addis Ababa, Ethiopia. To determine factors that affect time to return of donors, various parametric shared frailty models were compared. Donation sites were used as the clustering variable in all of the models. Exponentials, Weibull, log-logistic, and lognormal as baseline hazard functions and gamma and inverse Gaussians for the frailty distributions are used. The performance of all models was compared using the AIC criteria.

Results: A total of 6,019 voluntary blood donors donated blood during study period. The median return time of the donors was about 26 months. About 46.7% of the donors returned to donate blood again during the study period. The Lognormal model with Gamma frailty has the minimum AIC value among the models compared. Gender, age, weight, occupation, donation experience, and experience of the donors' reaction were significantly associated with the time to return of blood donors.

Conclusion: Being a male donor, being repeat donor, and increasing weight significantly minimize the time-to-return of blood donors, whereas being aged 45-65, being a student, and experiencing donors' reactions significantly prolong the time to return of volunteer blood donors. Policymakers and human resource managers are expected to develop appropriate donor motivational strategies to improve the time to return of blood donors.

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Keywords: Volunteer blood donors; Donors' Return

Abbreviations: AA: Addis Ababa; ADR: Adverse Donor Reaction; BDRR(s): Blood Donor Return Rate(s); ENBBS: Ethiopian National Blood Bank Service; FMOH: Federal Ministry of Health; Kg: Kilogram; NBTS: National Blood Transfusion Services; Rh: Rhesus; WHO: World Health Organization



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Introduction

Blood is the most valuable and unique gift that one person can give to another. It is a life-saving fluid that cannot be produced artificially and can only be obtained from donors, who are scarce resources [1]. All over the world, the demand for blood and blood products is growing [2]. Despite rising blood demand due to an increase in the number of clinical procedures requiring transfusions, the number of qualified volunteer blood donors is dropping. Due to this, there is a widespread shortfall between blood requirements and blood supplies in many countries [3].

Ethiopia's annual blood collection rate is far below its demand [4]. In this regard, a joint press conference held by the Ministry of Health and the National Blood Bank stated that the blood deficit had reached a critical stage over the period as less volume of donated blood was collected. Consequently, the Blood Bank was unable to supply the necessary volume of donated blood to hospitals and health centers, causing their patients to suffer even more [4]. In the end, ensuring an adequate and safe blood supply has become a major challenge in Ethiopia [5].

Since existing donors have less risk of blood infections and have less severe medical screening, focusing on preventing donors from the lapse or becoming inactive is an interesting strategy [6]. Hence, maximizing return rates and minimizing time intervals between donations yield a better supply of blood that keeps up with the increasing demand for blood and blood products [7]. So, in order to enhance the supply of safe and enough blood and blood products, studying the covariates of time to return (time gap between donations) of volunteer blood donors was found to be a predominant issue and it was one of the reasons for conducting this study. Knowing the time to return of a donor and its potential covariates enables the concerned body to adopt appropriate donor motivational strategies.

Some studies have been conducted to identify covariates of blood donor return using logistic regression [7-11] and Cox proportional hazard models [12-16]. However, logistic regression does not take censoring observations into account. Similarly, correct inference based on Cox's models requires samples that are identically and independently distributed. The Cox proportional hazards model did not account for any additional heterogeneity present in the data. Ignoring this heterogeneity will result in biased parameter estimates and inconsistent standard errors [17]. Consequently, this study used a shared frailty model to investigate the factors associated with the time to return of voluntary blood donors, while accounting for heterogeneity.

Methods and materials

Study design, Period and Area

A retrospective cohort study was conducted on all volunteer blood donors who donated blood from 06 September 2017 to 11 September 2018 and whether or not they returned was tracked until September 2018 at the National Blood Bank Service in Addis Ababa, Ethiopia. In Ethiopia, any healthy person between the ages of 18 and 65 who weighs at least 45 kg is eligible to donate. A donor must weigh at least 45 kg to donate 350ml and 50 kg to donate 450 ml [18].

The time taken to return was the time interval between the first two consecutive donation times during the study time, which had been rounded to the nearest month. Donors who do

not donate blood at least two times during the study time are considered censored. Thus, for the donors who returned, their follow-up was only until their first return.

Variables in the Study

The outcome variable considered in this study was the time to return of volunteer blood donors.

The explanatory variables considered in this study were: age of the donor (18-24, 25-44, 45-65), gender (female, male), weight (45-49, 50-59, 60-69, 70-79, 80), occupation (civil servant, private, student, unemployed, NGO worker), the volume of blood donated(350, 450), blood group (A, B, AB, O), Rh factor(negative, positive), donation experience(first time, repeat), experiencing the donor's reaction(no, yes), and donation site (mobile or fixed).

Shared frailty model

The shared frailty model extends the univariate frailty model by allowing individuals in the same cluster to have the same frailty value. When frailty is shared, individuals who share frailties become dependent on one another.

Depending on the random term called frailty w_i , the survival times in cluster i ($1 \leq i \leq n$) are assumed independent, the accelerated failure time frailty model assumes:

$$h_{ij}(t / X_{ij}, w_i) = ho(\phi t) \exp(\beta' X_{ij} + w_i) \quad (1)$$

Where; i indicates the i^{th} cluster, j indicates the j^{th} individual in the i^{th} cluster, $\phi = \exp(\beta' X_{ij} + w_i)$, $ho(t)$ is the baseline hazard, w_i the random term for all subjects in cluster i , X_{ij} is the vector of covariates for subject j in cluster i , and β is the vector of regression coefficients.

The variability in this model comes from two sources: natural variability, which is included in the baseline hazard function, and a frailty term, which represents the unobserved variability from the covariates [19].

To investigate the effect of the candidate covariates on the time-to-return of volunteer donors, we first did a univariable analysis by fitting a separate model for each candidate covariates. Covariates identified as significant in the univariable analysis were included in the multivariable analysis. The multivariable survival analysis in the study was done by assuming the exponential, Weibull, log-logistic, and log-normal distributions for the baseline hazard function; and the gamma and inverse Gaussian for frailty distributions.

Frailty distributions

Gamma distribution

It is very well suited to failure data in terms of computational and analytical points of view. It is widely used due to mathematical tractability [19]. Assuming a two-parameter gamma density with $\delta > 0$ and $\gamma > 0$ as shape and scale parameters respectively, the density function is given by:

$$f_z(Z) = \frac{\gamma^\delta Z^{\delta-1} \exp(-\gamma Z)}{\Gamma(\delta)} \quad (2)$$

with $\delta > 0$ and $\gamma > 0$ and where $\Gamma(\cdot)$ is the Gamma function.

In gamma frailty models, restriction $\delta=\gamma$ is used, which results in an expectation of 1. The variance of the frailty variable is then 1. Assuming that the frailty term z_i is a gamma with $E(Z) = 1$ and $Var(Z) = \theta$, then $\gamma = \frac{1}{\theta}$.

Larger values of, θ indicate that there is a higher degree of heterogeneity among groups and strong association within groups [17]. Then the density of a gamma-distributed random variable frailty term z_i with parameter θ is:

$$f_z(Z) = \frac{\gamma^\delta Z_i^\delta \exp(-\gamma\delta)}{\Gamma(\delta)} \quad (3)$$

Where: $\Gamma(\cdot)$ is the gamma function; it corresponds to a Gamma distribution $\text{Gam}(\mu, \theta)$ with μ fixed to 1 for identifiability and its variance is θ .

Inverse Gaussian distribution

Similar to the gamma frailty model, simple closed-form expressions exist for the unconditional survival and hazard functions, this makes the model attractive [20]. The probability density function of an inverse Gaussian distributed random variable Z with parameter $\theta > 0$ is given by:

$$f_z(Z) = \frac{\gamma^\delta Z_i^\delta \exp(-\gamma\delta)}{\Gamma(\delta)} \quad (4)$$

It has a mean one and variance θ

For comparison of different models, the AIC criteria were used. A model having a minimum AIC value is considered a better fit.

Results

Descriptive Statistics of the study participants

Of all 6,019 voluntary blood donors, the majority of the participants, 3847 (63.9%), were males. Donors aged 25-44 years accounted for 51.6% of the study participants. Nearly one-third (31.2%) of the participants weighted 50-59, followed by those who weighted 60-69 (30.0%). Private workers account for 61% of the participants who donated blood during study time. Nearly all (92.7%) of the donors had Rh-positive, and the majority of them (41.6%) had AB blood group. Donors who donated 350 (ml) accounted for 71.4% of the total. More than half (51.9%) of the participants donate blood at a fixed site. Nearly 97% of the donors had no donor reactions during blood donation (Table 1).

Multivariable analysis and comparison of models

For the time to return of volunteer blood donors, the exponential, Weibull, log-logistic, and lognormal multivariable survival models for the baseline hazard function; and the gamma and inverse Gaussian frailty distributions were fitted by taking all significant covariates in the univariable analysis. A model with a minimum AIC value was preferred. The AIC value of the Lognormal-Gamma shared frailty model, (AIC=25626.23), was the lowest of all the models, indicating that it was the most efficient model for describing volunteer blood donors' data set (Table 2).

The lognormal-gamma frailty model analysis revealed that the donor's gender, age, weight, occupation, donation experience, and the donor's reaction were significantly associated with the time to return of blood donors (Table 3). This indicates that they were the contributing factors in the time spent on returning blood donors. However, according to this model, the volume of blood donated and the blood group of the donors had no significant effect on the time to return of blood donors.

When the effect of other factors was kept fixed, male donors had a significantly different return time than female donors, with an acceleration factor of 0.481. Therefore, male donors had a shorter return time for the next donation by a factor of

Table 1: Descriptive summaries of the study participants.

Variable	Categories	Return Status		
		Never returned (%)	returned (%)	Total (%)
Gender	Female	1312(60.4)	860(39.6)	2172(36.1)
	Male	1896(49.3)	1951(50.7)	3847(63.9)
Age (in years)	18-24	1246(46.3)	1447(53.7)	2693(44.7)
	25-44	1857(59.8)	1247(40.2)	3104(51.6)
	45-65	105(47.3)	117(52.7)	222(3.7)
Weight (in Kg)	45-49	185(71.7)	73(28.3)	258(4.3)
	50-59	1204(64.1)	675(35.9)	1879(31.2)
	60-69	959(53.1)	848(46.9)	1807(30.0)
	70-79	564(45.2)	684(54.8)	1248(20.7)
Blood group	≥80	296(35.8)	531(64.2)	827(13.7)
	A	872(50.9)	841(49.1)	1713(28.5)
	B	781(54.7)	647(45.3)	1428(23.7)
	AB	215(57.6)	158(42.4)	373(6.2)
Rh	O	1340(53.5)	1165(46.5)	2505(41.6)
	Negative	235(53.5)	204(46.5)	439(7.3)
Occupation	Positive	2973(53.3)	2607(46.7)	5580(92.7)
	Civil servant	100(36.1)	177(63.9)	277(4.6)
	Private	1781(48.5)	1893(51.5)	3674(61.0)
	Student	1298(65.5)	684(34.5)	1982(32.9)
	Unemployed	5(13.9)	31(86.1)	36(0.6)
Volume of blood donated (ml)	NGO worker	24(48.0)	26(52.0)	50(0.8)
	350	2536(59.0)	1760(41.0)	4296(71.4)
Donation experience	450	672(39.0)	1051(61.0)	1723(28.6)
	1 st time donor	913(51.9)	846(48.1)	1759(29.2)
Donation site	Repeat donor	2295(53.9)	1965(46.1)	4260(70.8)
	Mobile	1994(68.8)	904(31.2)	2898(48.1)
Donors' reaction	Fixed center	1214(38.9)	1907(61.1)	3121(51.9)
	No donor reaction	3086(52.9)	2753(47.1)	5839(97.0)
Donors' reaction	Donor reaction	122(67.8)	58(32.2)	180(3.0)

Table 2: AIC values of the models used in the study.

Baseline hazard function	Frailty distribution	AIC
Exponential	Gamma	26267.97
	Inverse-Gaussian	26261.01
Weibull	Gamma	26158.96
	Inverse-Gaussian	26148.93
Lognormal	Gamma	25626.23
	Inverse-Gaussian	25638.24
Log logistic	Gamma	25822.55
	Inverse-Gaussian	25822.53

0.481 than female donors. Donors aged 45-65 years had a significantly different return time than donors aged 18-24 years with an acceleration factor ($\phi = 1.283$). Hence, they had a prolonged return time for the second donation by a factor of 1.283 compared to donors aged 18-24.

Table 3: Lognormal- Gamma multivariable analysis.

Variable	Categories	Coef	S.E	ϕ	95% CI	p-value
Gender	Female	Ref.				
	Male	-0.731	0.0519	0.481	[0.435 0.731]	0.016
Age (in years)	18-24			1		
	25-44	0.0931	0.0559	1.098	[0.984 1.225]	0.096
	45-65	0.2493	0.1252	1.283	[1.004 1.640]	0.047
Weight (in Kg)	45-49			1		
	50-59	-0.1263	0.1262	0.881	[0.688 1.129]	0.32
	60-69	-0.3607	0.1294	0.697	[0.541 0.898]	0.005
	70-79	-0.4111	0.1364	0.663	[0.507 0.866]	0.002
	≥80	-0.5801	0.1427	0.56	[0.423 0.740]	<.001
Blood group	A			1		
	B	0.0999	0.0623	1.105	[0.978 1.249]	0.11
	AB	0.1489	0.1006	1.161	[0.953 1.414]	0.14
	O	0.0523	0.0542	1.054	[0.947 1.172]	0.33
Occupation	Civil servant			1		
	Private	0.0799	0.1049	1.083	[0.882 1.330]	0.45
	Student	0.3857	0.1156	1.471	[1.173 1.845]	<.001
	Unemployed	-0.1736	0.2815	0.841	[0.484 1.460]	0.54
	NGO worker	0.3319	0.2602	1.394	[0.837 2.321]	0.2
The volume of blood donated (ml)	350			1		
	450	0.0498	0.0567	1.051	[0.940, 1.175]	0.38
Donation experience	1 st -time donor			1		
	Repeat donor	-0.9027	0.0621	0.405	[0.359 0.458]	<.001
Experiencing donors' reaction	No			1		
	Yes	1.6516	0.1470	5.215	[3.909 6.957]	<.001

$$\theta = 1.1 \lambda = 1.54, AIC = 25626.23, \tau = 0.523,$$

Source: National Blood Bank Service, A.A, Ethiopia; donated blood from 06 September 2017 and 11 September 2018 and whether he/she returned or not, would be followed until September 2020, Coef=coefficients of the model, SE=Standard error, ϕ =Acceleration factor, CI=confidence interval for ϕ , θ =Variance of the random effect, τ =Kendall's tau, λ =Scale

Given the effect of other factors kept constant, donors with weight (60-69, 70-79, and ≥ 80) had significantly different return times than donors that had weight 45-49 with an acceleration factor of 0.697, 0.663, and 0.56 respectively. Therefore, donors with a weight (in Kg) of 60-69, 70-79, and ≥ 80 had a shorter return time for the next donation by a factor of 0.697, 0.663, and 0.56 respectively than the reference group 40-49. From this, we understand that as the weight increases, the time required for the next donation decreases.

According to the results, the type of occupation that the donors had was known to be a significant covariate. Donors with the occupation of students had a significantly different return time for the next donation than civil servants, with an acceleration factor of 1.471 and a 95% confidence interval of [1.173, 1.845]. This result suggested that students had a prolonged time to the next donation than civil servants.

The donation experience of blood donors had a significant effect on the time of the return of the blood donors. According to the results, repeat blood donors had a significantly different return time than the 1st time donors with an acceleration factor of 0.405. This indicates that repeat blood donors return to the hospital sooner than first-time donors.

Providing the effect of other factors was kept constant, donors who experienced donors' adverse reaction had a significantly different return time for their next donation than donors who didn't experience donors' adverse reaction, with an acceleration factor of 5.215 and a 95% confidence interval of [3.909, 6.957]. This result suggested that donors who experienced donors' adverse reactions had an extremely longer (5.215) time to return for the next donation than those who didn't experience donors' adverse reactions.

Survival of significantly different groups

The survival time to return for donors who experienced an adverse reaction (red line) is greater than for those donors who didn't experience an adverse reaction (green line). This implies that the survival time to return of donors who did not have an adverse reaction is longer than that of donors who did (Figure 1).

Adverse reaction status of donors KM

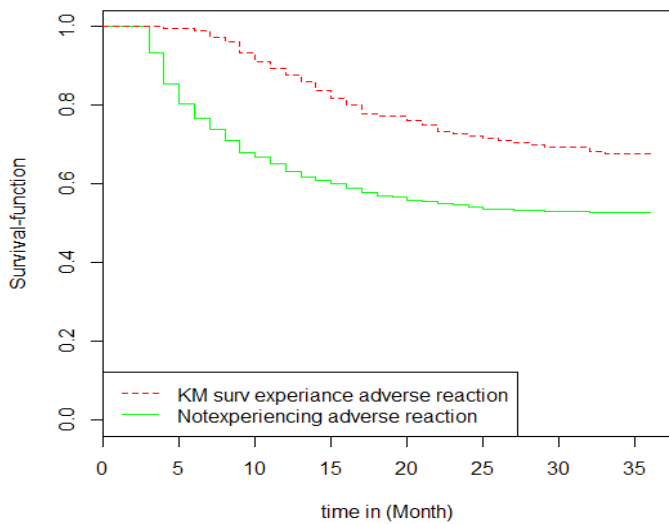


Figure 1: The survival functions of adverse reaction status of donors using the Lognormal-Gamma frailty model.

To check the adequacy of our baseline hazard: - Exponential is plotted by $-\log(\hat{s}(t))$ versus t ; Weibull is plotted by $\log(-\log(\hat{s}(t)))$ versus $\log(t)$; Log-logistic is plotted by $\log\left(\frac{1-\hat{s}(t)}{\hat{s}(t)}\right)$ versus $\log(t)$ and Log-normal baseline plotted by of $\Phi^{-1}\{1 - \exp(-H(t))\} = \Phi^{-1}\{1 - \hat{s}(t)\}$ versus \log time (t). The plot of lognormal is slightly more linear than the other plots (**Figure 2**). The patterns suggest that the lognormal hazard function is appropriate in the model.

lognormal

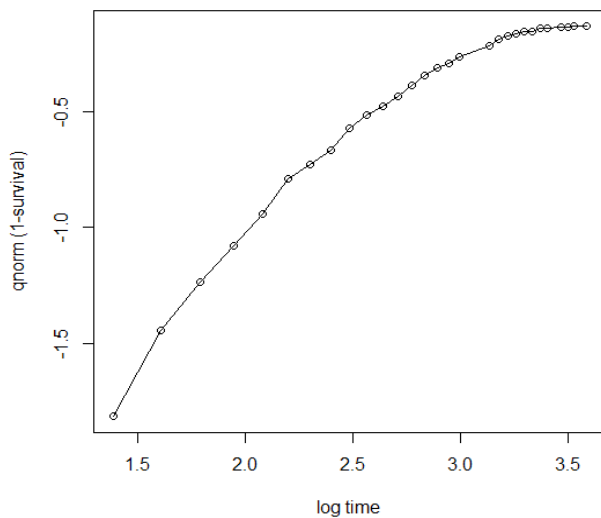


Figure 2: Graphical evaluation of the log-normal assumptions.

The Cox Snell residual plots

The Cox-Snell residuals are one way to investigate how well the model fits the data. In this case, we used the Cox-Snell residuals to check the overall goodness of the fit for different parametric models. The Cox-Snell residuals were obtained by fitting the lognormal model to our data via maximum likelihood estimation. In comparison to the Exponential, Weibull, and Log logistic models, the Lognormal model's plot of Cox-Snell residuals was closest to the line through the origin, indicating that this model best describes the donors' dataset (**Figure 3**).

Cox snell for lognormal

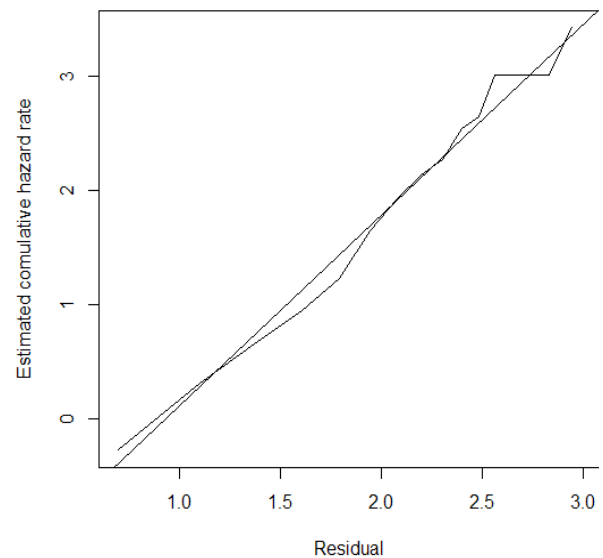


Figure 3: Cox-Snell residuals that were obtained by fitting log-normal to the donors' dataset.

Adequacy of accelerated failure time

A quantile-quantile or q-q plot is used to determine whether the accelerated failure time provides an adequate fit for the data using two different groups of the population. We shall graphically check the adequacy of the accelerated failure-time model by comparing some significantly different groups, like reaction status (experience an adverse reaction, not experiencing adverse reaction), donation experience (1st time or repeat donors), and gender of the donors (**Figure 4**). For all covariates, the figures appear to be approximately linear. Therefore, the accelerated failure time model using lognormal as a baseline was best to describe the donors' data set.

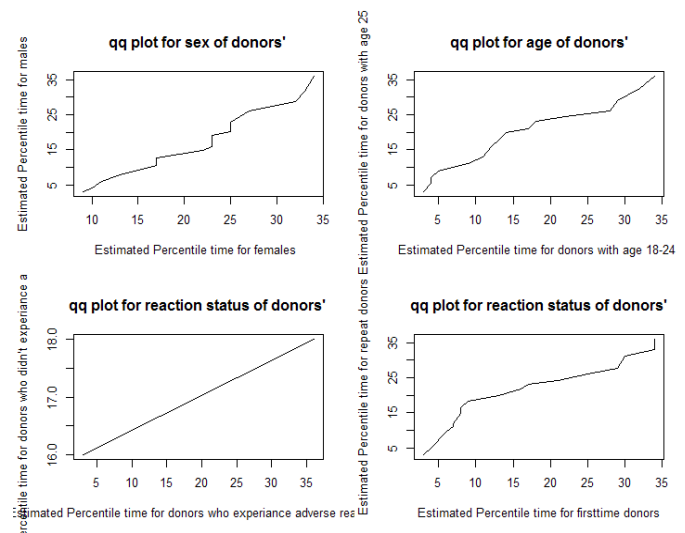


Figure 4: Q-Q plots to check the adequacy of the accelerated failure time model.

Discussion

The primary goal of this study was to predict the time it would take for volunteer blood donors to return to the National Blood Bank in Addis Abeba, Ethiopia. From a total of 6,019 voluntary blood donors, only 2811 (46.7%) returned to donate blood one or more times during the study period. This result is small as compared with the findings of Kasraian & Tavassoli, et al, whose return rate was 51.7% during the 3 years after the first donation

[21]. Similarly, it is lower than the findings of a study conducted in the Netherlands, where the return rate after nearly a year is 82% without adverse reaction [9]. On the other hand, it is much better than the study findings by Fantahun. et.al, found that the return rate among first-time blood donors for subsequent donations was 37.7% per two years [10].

The Lognormal-gamma shared frailty model has a minimum AIC value selected as the best fit for the donors' data set. This study also showed that there was a significant clustering (frailty) effect on the modeling time to return of volunteer blood donors, which is due to the heterogeneity between the donation sites where they donate blood. Heterogeneity in the donation sites was estimated to be $\theta=1.1$, and the dependence within clusters was about ($\tau = 0.523(52.3\%)$). Those values were the maximum between the variance of the random effects and Kendall's tau of all the candidate models. This finding supports the notion that higher values indicate greater heterogeneity among groups and strong associations within groups [17].

Even though the most well-known parametric model is Weibull, which allows for proportional hazards and an accelerated failure time model [22], the log-normal baseline described the donors' data set better than the exponential, Weibull, and Log logistic hazard functions. According to the diagnostic plots, the log-normal ($1 - (\Phi^{-1}) \{1 - \hat{S}(t)\}$ versus log time) the plot was slightly more linear than the plots of exponential (cumulative hazard versus time), Weibull (log cumulative hazard versus log time), and Log logistic (log failure odds versus log time), indicating that the log-normal baseline best described the donors' dataset. The cumulative hazard plots for the Cox-Snell residuals of the exponential, Weibull, log-normal, and log-logistic models confirmed this result. The plot was very close to the line in the case of the log-normal model, indicating that it was the best.

The best model, the log normal-gamma frailty model, revealed that the donors' gender, age, weight, occupation, donation experience, and experienced donors' reaction were significant predictor factors of time to return of volunteer blood.

The results of our findings showed that male donors had a shorter return time for the next donation by a factor of 0.481 than female donors. Similar findings, such as Wevers et, al and Notari Iv et, al, have been reported in the literature [23] [24]. More men tend to be repeat donors than women [21]. In contrast to this finding, a study found that being a female donor was associated with subsequent blood donations [13]. Even though gender influences donor returns in the literature, including our findings, [25] and [15] concluded that the effect of gender on donors is not statistically significant.

When comparing donors aged 45 to 65, the period it took them to return was 1.23 times longer as compared to donors of age 18-24. The age of the donor has a negative impact on the time intervals between donations: the younger the donor, the shorter the time intervals between donations, and thus the greater the likelihood of future donations [7]. Donors under the age of 19 are more likely than older donors to make multiple donations [26].

In contrast to the presented literature, [13] and [23] discovered that increasing age was positively associated with subsequent visits. Return rates were lowest among the age groups of 18-24 years, then gradually increased with age [13].

According to the findings of this study, the higher the weight, the greater the likelihood of returning to donations and the

shorter the time interval between donations. The weight of repeat donors was greater than that of first-time donors [13] [7].

Donors who experienced an adverse reaction took 5.215 more times to donate blood than those who did not experience an adverse reaction. Complications either reduce donor returns or increase the time it takes to return the donation [9,12,27]. In contrast to our findings, a study conducted in Australia discovered that donor reactions do not always deter donors from continuing to donate [28].

According to the findings of this study, repeat donors took 0.405 fewer times to return than first-time donors. Those with a higher return rate appeared to return more frequently [23]. Donors with one previous donation had 3.7 times the odds of future return as first-time donors [29]. According to a study conducted in Brazil, 43.8 percent of those who donated five or more times returned for the next donation in less than six months. This could be related to the fact that donors who make donations are more likely to do so again [30].

The donor's occupation was identified as a significant factor in the time it took for volunteer blood donors to return. The result shows the return time for donors who were students is 1.471 times longer (less likely to return) than for civil servants. Despite the fact that university students are in the age range for a large pool of blood donors, the proportion of students who have ever donated blood is extremely low [31]. In contrast to our findings, a study conducted by Kheiri et al discovered that university students had a higher chance of donating than others, such as housekeepers [7].

Conclusion

The model that best describes the time to return of the donors' dataset is the Lognormal-gamma shared frailty model. There is a frailty (clustering) effect on the time-to-return of donors that arises due to heterogeneity between donation sites. The median return time of the donors was about 26 months, with a maximum return time of 36 months. The analysis based on the Lognormal-gamma frailty model shows that being a male, donation experience (repeat donor), and increasing weight (in Kg) significantly shorten/minimize the time-to-return of blood donors while being in the age group (45-65), being a student and experiencing donors' reactions prolongs the time-to- the return of volunteer blood donors. Policymakers and human resource managers are expected to establish appropriate policies, programs, and donor motivating tactics for those groups with a long return time.

Ethics approval and consent to participate

Ethical clearance for this study was obtained from the Jimma University Institute of the research review board. The author requested access to the data from National Blood Bank Service and access was granted to use the data for this study.

Consent for publication: Not applicable

Funding: There is no funding available.

Availability of data and materials

In return for a reasonable request, the corresponding author will provide you with the datasets used in this study.

Competing interest

The authors state that they have no competing interests.

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