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Time to initiation of antenatal care and its predictors among Ethiopian women: Multilevel Mixed-effects Acceleration Failure Time model

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Abstract

Background: Pregnancy-related preventable morbidity and mortality are still at unacceptable levels at the start of the Sustainable Development Goals era. On the top of negative correlation with maternal morbidity, ANC has positive correlation with health facility delivery.Yet, in Ethiopia, the rate of early ANC initiation ranges from 21.71% in the south to 46.8% in the north.Thus, this study aimed to identify the time-to-initiation of ANC and its predictors in Ethiopia using a nationally representative survey data.

Methods:This study included a weighted sample of 2933 women aged 15 to 49 who had an ANC visit for their most recent child within the five years prior to the survey and whose gestational age was known at the first antenatal visits. To investigate the individual and communal factors that influence the timely initiation of ANC, a multilevel mixed-effects Weibull distribution survival regression model was fitted. The Adjusted Acceleration Factor (AAF) with its 95% confidence interval (CI) was applied to present the findings.

Results: In this study, the estimated mean survival time of pregnant women to initiate the first ANC visit in Ethiopia was found to be 6.8 months (95% CI: 6.68, 6.95).Women whose last birth was a caesarean section (AFT = 0.72; 95% CI: 0.63, 0.82), women who have media access (AAF = 0.90; 95% CI: 0.81, 0.99), and women with higher education (AAF = 0.71; 95% CI: 0.59, 0.85) and women with primary education (AAF = 0.89; 95% CI: 0.80, 0.98)had a shorter time to initiate ANC early in the first trimester of pregnancy.However, being grand multiparous (AAF = 1.19; 95% CI: 1.02, 1.39), being previously in a union (AAF = 1.43; 95% CI: 1.14, 1.78), having a home birth (AFT = 1.34; 95% CI: 1.20, 1.49), and living in a rural area (AAF = 1.20; 95% CI: 1.01, 1.43) were the impediments for early ANC initiation.

Conclusion: Women in this study area sought their initial antenatal care far later than the WHO recommended.It's crucial to provide health education with a focus on empowering expectant mothers to timely activate prenatal care, especially for those who give birth at home and for those who reside in remote areas. Expanding health education through the use of media should also be a part of initiatives to boost the timely initiation of antenatal care utilization.

Keywords: antenatal care, mixed-effects model, acceleration failure time, Ethiopia

Strength and limitations of this study

- This study employed a multilevel mixed-effects parametric survival model to identify predictors of infant mortality.
- This study used a large sample from nationally representative survey data to identify both individual-level and community-level predictors.
- The study used retrospective birth history data to analyze infant mortality, and is likely to suffer from mothers' recall bias.

Introduction

A healthy pregnancy for both mother and child, a smooth transition to a happy labor and delivery experience, and successful parenthood are all aspects of the positive pregnancy experience that women want and need(1). However, the morbidity and mortality rates associated with pregnancy that are preventable are still too high at the outset of the Sustainable Development Goals (SDG) period. In order to improve the pregnancy's outcome, antenatal care (ANC) is a crucial time for health promotion, screening, and disease prevention(2). ANC exhibits a positive link with delivery in a medical facility on top of the negative correlation with maternal morbidity(3).

Early detection of modifiable risk factors and pre-existing conditions is made possible by timely prenatal care initiation, which is defined as the first antenatal contact taking place during the first trimester of pregnancy(4). The 2016 World Health Organization (WHO) recommendation also suggests early beginning of ANC within the first 12 weeks of gestation(2). Women with early ANC initiation are more likely to have sufficient amount of antenatal care contacts(5).

There has been a significant improvement in the estimated global coverage of early prenatal care visits, going from 40.9% in 1990 to 84.8% in 2013, or a 43.3% increase(4).The Estimated coverage of early prenatal care visits in low-income countries (LMICs) in 2013 was 24 percent, compared to 81 percent in high-income countries(4).Data from these nations' Demographic Health Surveys (DHS) from 2012 to 2018 show that this percentage has climbed to 44.3% (5). Yet, this shows that the rate of early initiation of ANC in the LMICs is very far from the optimal level.

A woman dies every two minutes due to pregnancy or childbirth according to United Nations (UN) estimates(6).The poorest nations and those experiencing conflict continue to have the highest rates of maternal fatalities. With 3.6% of all maternal deaths worldwide in 2020, Ethiopia had the fourth-highest estimated number of maternal deaths, behind Democratic Republic of the Congo, Nigeria, and India(6). Timely ANC initiation is essential to lowering maternal morbidity and mortality in countries with high rates of maternal morbidity and mortality(7).

The magnitude timely initiation of ANC visit in Sub-Saharan Africa was 38.0%, ranging from 14.5% in Mozambique to 68.6% in Liberia(8). In Ethiopia, being one of the SSA countries, the problem is even worse. The median time to antenatal care initiation in the country was found to be 5 months(9). The result from 2016 Ethiopian Demographic Health Survey (EDHS) revealed only 20% of pregnant women in Ethiopia start their ANC during the first trimester of their pregnancy(10). Other studies in the country reported varying magnitude of early initiation of ANC; the proportion was found to be 46.8% in Bahirdar(11), 21.71% in southern Ethiopia(12), 40.6% in Debre Markos(13), 39.5% in Tselemt district of Tigray Region(14), 27.5% in Axum(15), 28.8% in Ilu Ababor(16), 34% in Bench-Sheko zone(17).

Predictors of timing of first antenatal care follow up from different literatures were residence(18)(10)(19), household wealth(20)(18), educational status of the women(18)(21)(15), media exposure(19)(21)(18), occupation of the women(22)(23)(24), parity(21)(25)(26), husband education(20)(19), husband occupation(19), distance from health facility(26)(18)and maternal age(20)(18)(27).

Despite various studies on identifying risk factors for time to first ANC follow-up were conducted in Ethiopia, only few studies found to be representative at the national level. Furthermore, almost all of the studies failed to consider community-level factors for time to initiation of ANC in Ethiopia. Updated and nationally representative information is very crucial for policy makers and other concerned bodies to improve the level of early antenatal care initiation. Therefore, this study undertook a retrospective analysis based on the 2019 Ethiopian Mini Demographic and Health survey (EMDHS) data set, to identify time-to-initiation of ANC and its predictors in Ethiopia.

Methods

Study design and area

This study undertook a retrospective analysis based on the 2019 Ethiopian Mini Demographic and Health survey (EMDHS) data set. Ethiopia is located in the Horn of Africa and shares a border with Eritrea, Djibouti, Somalia, Sudan, South Sudan, and Kenya. It is the second most populous nation in Africa, with over 110 million populations(28). Based on the 2021 World Bank reports Ethiopia had a gross national income per capital of US$ 940(29).

Source of data

The data were obtained from EMDHS 2019, specifically the under-five children's file (KR)

(http://www.measuredhs.com). The unweighted sample consisted of 5753 women who had live births in the five years preceding the survey. The 2019 EMDHS sample was stratified and selected in two stages, and interviews were conducted face-to-face with permanent residents and visitors who stayed in the residences the day before the survey. The 2019 EMDHS sampling frame is a composite of all census enumeration areas (EAs) created for the upcoming 2019 Ethiopia Population and Housing Census (PHC) conducted by the Central Statistical Agency (CSA). The census frame includes the complete list of 149,093 EAs created for the 2019 PHC. An EA is a geographical area with an average of 131 households. The sampling frame includes data on the EA's location, type of residence (urban or rural), and the estimated number of residential households(30).

Study population

The study included pregnant women aged 15–49 years old whose gestational age was known at the first Antenatal visits. Women who had ANC visits but whose gestational age at the time was unknown (unrecorded) were excluded from this study.

Study variables

Outcome of interest

The dependent variable is time-to-first ANC receipt among pregnant women which is measured in months. The event of interest considered as success (event = 1) if women had antenatal care in the first trimester of pregnancy and otherwise censored (censored = 0).

Independent variable

Individual level factors were women education level, household wealth index, birth interval, number of antenatal care visit, age of the women, media exposure and marital status.

Community level factors were residence, region, community educational status, communityANC coverage and community poverty. The EMDHS did not collect data that can directly describe the clusters' characteristics except the place of residence and region. Therefore, other common community-level data were generated by aggregating the individual characteristics with our interest in a cluster. The aggregates were computed using the proportion of a given variables'

subcategory we were concerned on in a given cluster. Since the aggregate value for all generated variable was not normally distributed. It was categorized into groups based on the national median values.

Operational definition

Exposure to mass media: a frequency of listening to the radio and watching television were considered exposure to mass media in this study by excluding exposure to magazines and newspapers. So, women exposed to either television or radio at least once per week considered exposed, if not exposed at all, taken as not exposed.

Community women education: Was defined as the proportion of mother's who attended primary/secondary/ higher education within the cluster. The aggregate of individual mother's primary/secondary/higher educational attainment can show the overall educational status of women within the cluster. There were two categories for this variable with reference to the national median value: higher proportion of mother's who attended primary/secondary/higher education and lower proportion of mother's who attended primary/secondary/higher education within the cluster.

Antenatal care utilization: was defined as mothers who had at least four antenatal care visit(2).

Community antenatal coverage: The proportion of women in the clusters who had four and above antenatal care (ANC) from a skilled provider during the pregnancy of last delivery.

Community poverty status: It is defined as the proportion of poor or poorest mothers within the cluster. Within the cluster proportion of poor or poorest were aggregated and show over all poverty status within the cluster.

Data Quality Control and Assurance

The data sets for the original work were collected by face-to-face interviewing women using structured questionnaires that met the eligibility criteria. The woman's questionnaire, the household questionnaire, and the Health Facility Questionnaire were employed to gather essential information. After the questionnaires were finalized in English, they were translated into Amarigna, Tigrigna, and Afaan Oromo. In addition to this, the gathered data was back-translated into English to keep consistency. The quality of the dataset has maintained by testing its completeness. Moreover, the quality of the original data set was maintained by giving training to interviewers, and interviewers used tablet computers to record responses during the interviews.

For this study, the data were weighted using sampling weight before any statistical analysis to restore the representativeness of the data and to get a reliable estimate and standard error. The weighted results from the analysis were reported in the study. Multicollinearity between independent variables was checked using Variance Inflation Factor (VIF) and the mean VIF was 2.11. The proportional hazards (PH) assumption was tested using Scaled Schoenfeld residuals and found to be unsatisfied, with a global test value of 0.0001. The data was also assessed for an interaction factor.

Data Management and Analysis

STATA version 14 software was used for cleaning, recoding, and analyzing the data. Descriptive statistics were applied using frequencies and percentages. Estimation of survival probability was done by using the Kaplan Meier survival curve. Survival curves were compared by log-rank test. Univariate survival regression was fitted for explanatory variables and those having p-value ≤0.25 level of significance were considered for the multivariable analysis. Then, the study applied a stepwise backward variable selection procedure to obtain the final reduced model. Finally, a multivariable mixed-effects parametric Weibull distribution survival regression model was fitted. Adjusted Acceleration Factor (AAF) with its 95% confidence interval (CI) was applied, and covariates with a P-value <0.05 in the multivariable analysis were considered determinants of the survival time to first ANC visit.

Survival analysis

Survival analysis deals with the analysis of survival data, which is used to measure the time to an event of interest, such as death or failure. The survival times for subjects who left the study early or who finished it without experiencing the event of interest are censored. Each uncensored observation is taken to indicate an event or death(31).

Let T denote the random variable for the survival time of a subject. Assume f(t), t≥0, denote the probability density function (pdf) of T, and let F(t)=P(T≤t), t≥0, be the cumulative distribution function (CDF) of T. The distribution of T is called the survival time distribution. The survival function, S(t), is defined as the probability that a subject survives up to time t(31):

$$S(t) = P(T > t) = 1 - F(t),\ t \geq 0 \quad \text{.....1}$$

Mixed-effects parametric survival analysis

The EMDHS used a multistage cluster sampling technique, whereby data were hierarchical (i.e., mothers and infants were nested within households, and households were nested within clusters). Considering the hierarchical nature of EMDHS data, mothers and infants who lived within the same cluster may have had similar characteristics to other mothers and infants compared to those in other parts of the country. Considering the clustered sampling approach, a two-stage multivariable mixed-effects parametric survival regression analysis was used to estimate the effects of individual and community level determinants on infant mortality.

Mixed-effects survival models contain both fixed effects and random effects. Random effects are useful for modeling intracluster correlations; that is, observations in the same cluster are correlated because they share common cluster-level random effects. Mixed effects parametric survival model makes the often more plausible assumption that random effects are normally distributed, meaning frailties are lognormal. It also helps to extend the types of models that we can fit beyond two-level models with random intercepts(32).

Parametric survival mixed-effects models use a trivariate response variable (t0; t; d), where eachresponse corresponds to a period under observation (t0; t] and results in either failure (d = 1) orright censoring (d = 0) at time t. Accelerated Failure Time (AFT) model is a model used for adjusting survivor functions for the effects of covariates. In the AFT parameterization, the natural logarithm of the survival time, log *t*, is expressed as a linear function of the covariates(31):

$$\log(t_j) = X_j\beta + Z_j u_j + v_j \quad \ldots\ldots 2$$

for j = 1, . . . , M clusters with cluster j consisting of i = 1, . . . , nj observations. The vector x_{ji} contains the covariates for the fixed effects, with regression coefficients (fixed effect) β. The

vector z_{ji} contains the covariates corresponding to the random effects uj.**v***ji*are observation-level errors with density $\phi(\cdot)$. The distributional form of the error term determines the regression model. Five regression models are implemented in mestreg using the AFT parameterization: exponential, gamma, loglogistic, lognormal, and Weibull. Therefore, this study fitted a random-effects Weibull model with normally distributed random effects. This model can be viewed as a shared frailty model with lognormal frailty.

Four models were fitted to identify community and individual level factors associated with infant death. The first model (Model 1 or empty model) contained no explanatory variables. The second model (Model 2) considered only the individual-level variables in order to examine the individual-level effect. The third model (Model 3) considered only the community-level variables in order to examine the effect of community-level factors on infant death, independent of other factors. The fourth model (Model 4) is the full model that incorporated all individual and community-level variables into the multilevel analysis. Backward stepwise parametric survival regression analysis was performed to select individual and community-level variables for each model, and then all those selected variables were incorporated in to the multilevel modeling.

The fixed effect sizes of individual and community-level determinants of the survival time to first ANC visit were expressed as AAFs with 95% CI. The P-value <0.05 has been considered as statistically significant. Additionally, the measure of variance (random effects) was reported in terms of the intraclass correlation coefficient (ICC), median acceleration factor (MAF), and proportional change in variance (PCV).

ICC is a measure of within-cluster variation, the variation between individuals within the same cluster, and it was calculated using the formula(33):

$$ICC= (\delta_A)/(\delta_A + \pi^2/3) \quad \text{.....3}$$

Where δ_A is the estimated variance in each model, which has been described elsewhere. The total variation attributed to individual or/and community level factors in each model were measured by the proportional change in variance (PCV), which was calculated as(33):

$$PCV = (\delta_A - \delta_B)/(\delta_A) \quad \text{.....4}$$

Where δ_A = variance of the initial model, and δ_B = variance of the model with more terms. The MAF is the median acceleration factor between the individual of higher propensity and the individuals of lower propensity when comparing two individuals from two different randomly chosen clusters, and it measures the unexplained cluster heterogeneity, the variation between clusters by comparing two persons from two randomly chosen different clusters. It was computed using the formula:

$$MAF = \exp(\sqrt{2} * \delta A * 0.6745) \quad \text{.....5}$$

Where δ_A is the cluster level variance. The MAF measure is always greater than or equal to 1. If the MAF is 1, there is no variation between clusters(31).

The best fit model selection

Model fitness was checked using Akakian Information Criteria (AIC) and Deviance Information Criteria (DIC). The lowest AIC and DIC values declare the best fit model(31).

Result

Descriptive statistics

A total of **2933 (un weighted)** women were followed for a minimum of 1 and a maximum of 10 months with an average follow up time of 4 months. In this study, timely initiation of ANC visit in Ethiopia was found to be 42.7% (95% CI: 41.0 – 44.6). The estimated mean (restricted)

survival time of pregnant women to initiate the first ANC visit was 6.8 months (95% CI: 6.68, 6.95). The overall incidence rate was approximately 11 per 100 person month of observation.Majority 2755 (94.2%) of women were currently married or inunion, and of these 1030 (37.4%) had initiated ANC visit early in the first trimester of pregnancy. Regarding women education, 1283 (43.9%) women had no education, and among these 404(31.5%) initiated their ANC visit timely. Access to media was reported by 1259(43.1%) of whom 582(46.2%) had started ANC visit within 12 weeks of pregnancy. More than half 114(58.5%) of women who gave birth by C/S started their first ANC visit within the first trimesterTable 1.

Most 2052(70.2%) of the women were rural residents, and among these only 647(31.5%) women initiated ANC visit within the recommended time. The proportion of women starting first ANC visit within the first trimester was higher in Harari (66.7%), Dire Dawa (66.7%) and Addis Ababa (65%), whereas lower in the SNNPR (28.8%), Oromia (33.2%) and Somali (33.3%) regional states. More than half 1577(53.9) of the women were from a community with a low poor proportion of whom 740(46.9%) commenced their first ANC visit in the first three months of pregnancy. Moreover, 353(26.2%) women from a community with a high poor proportion commenced their first ANC visit timely Table 1.

Table 1 Summary of individual and community level factors of time to ANC initiation among study participants (2924), 2022

Covariates	Categories	Time to ANC initiation		Total N (%)
		Event N (%)	Censored N (%)	
Maternal education	Higher	105(68.6)	48(31.4)	153(5.2)
	Secondary	130(38.8)	205(61.2)	335(11.5)
	Primary	452(39.2)	701(60.8)	1153(39.4)

	No education	404(31.5)	879(68.5)	1283(43.9)
Wealth Index	Rich	647(48)	701(52)	1348(46.1)
	Middle	182(31)	407(69)	589(20.1)
	Poor	264(26.7)	723(73.3)	987(33.8)
Household size	1-5	692(43.3)	907(56.7)	1599(54.7)
(members)	6 or more	401(30.3)	924(69.7)	1325(45.3)
Maternal age	<20 years	48(31.4)	105(68.6)	153(5.2)
	20-34 years	846(39.2)	1310(60.8)	2156(73.8)
	≥35 years	199(32.4)	416(67.6)	615(21)
Household head	Female	156(40.4)	230(59.6)	386(13.2)
	Male	937(36.9)	1601(63.1)	2538(86.8)
Place of delivery	Facility	801(42.4)	1088(57.6)	1889(64.6)
	Home	292(28.2)	743(71.8)	1035(35.4)
PNC	No	881(36.5)	1532(63.5)	2413(82.5)
	Yes	212(41.5)	299(58.5)	511(17.5)
Last birth C/S	No	804(34.9)	1502(65.1)	2306(92.2)
	Yes	114(58.5)	81(41.5)	195(7.8)
Birth interval	≥36 months	478(37.6)	792(62.4)	1270(57.2)
(2220)	<36 months	305(32.1)	645(67.9)	950(42.8)
Ever had a child	No	939(39.7)	1429(60.3)	2368(81)
loss	Yes	154(27.7)	402(72.3)	556(9)
Parity	Primi-para	299(43.4)	390(56.6)	689(23.6)
	Multipara	559(40.8)	811(59.2)	1370(46.8)
	Grand Multipara	235(27.2)	630(72.8)	865(29.6)
Residence	Urban	445(51)	427(49)	872(29.8)
	Rural	647(31.5)	1405(68.5)	2052(70.2)
Community ANC	High	718(43.3)	937(56.6)	1655(56.6)
utilization	Low	375(29.6)	894(70.4)	1269(43.4)
Community	High	696(39.7)	1056(60.3)	1752(59.9)
women education	Low	397(33.9)	775(66.1)	1172(40.1)

Community level poverty	Low	740(46.9)	837(53.1)	1577(53.9)
	High	353(26.2)	994(73.8)	1347(46.1)

Comparison of the different covariate in terms of survival time to first ANC visit

Kaplan Meier graphs are generated to observe the difference in the survival time to first ANC visit of women for different categorical variables. The log-rank test was carried out to validate the difference between the groups of each categorical variable. The log-rank test result (Table 2) shows that there is statistically significant difference in the survival experience of groups among women education level ($p < 0.0001$), wealth index ($p < 0.0001$), delivery place ($p < 0.0001$), parity ($p < 0.0001$), media access ($p < 0.0001$), region ($p < 0.0001$), women age ($p < 0.001$) and Marital status ($p < 0.2$)Table 2.

Table 2 Comparison of survival time of individual and community level factors of time to ANC initiation among study participants (2924), 2022

Covariates	Categories	Time to ANC initiation		Log-rank test	P-value
		Event observed	Event expected		
Mothers education	No education	404	488	114.88	0.0001
	Primary	452	431		
	Secondary	131	126		
	Higher	105	47		
Household size	<6 members	692	585	54.22	0.0001
	≥6 members	400	507		
Ever had a child loss	No	938	876	28.21	0.0001
	Yes	154	216		
Women age	<20 years	49	57	11.48	0.0032

	20-34 years	845	802		
	≥35 years	198	233		
Birth interval	≥36 months	477	442	8.49	0.0036
	<36 months	305	340		
PNC	No	881	909	6.82	0.0090
	Yes	211	183		
Marital status	Currently in union	1030	1029	4.53	0.1039
	Formerly in union	54	59		
	Never in union	8	4		
Household head	Female	156	140	2.68	0.1018
	Male	936	952		
Community level	Low	739	569	136.88	0.0001
poverty	High	353	523		
Residence	Urban	445	310	105.30	0.0001
	Rural	647	782		
Community ANC	High	717	606	58.21	0.0001
utilization	Low	375	486		
Community	High	695	645	12.27	0.0005
women education	Low	397	447		

Random effects and model comparison

As the multilevel mixed-effects Weibull survival regression analysis results described inTable 3, Model I revealed statistically significant variation in the survival time to first ANC visit of women across communities. Nearly One fifth of the variation in the survival time is attributed to community-level factors (ICC = 18.9%). After adjusting the model for individual-level factors (Model II), about 32.2% of the variation in the accelerations of survival time was attributed to the individual level factors (PCV = 32.2%), and 13.7% of the variance in the survival time was attributed to community-level factors (ICC = 13.7%). Model III, which was adjusted for community-level factors, revealed that the community level factors explained 4.5% of the

variability in the accelerations of survival time to first ANC visit of women (PCV = 4.5%), and 13.1% of the variation among the clusters was attributed to community-level factors (ICC = 13.1%)Table 3.

The final best-fit model (model IV) was adjusted for both individual and community-level factors simultaneously. In this final model (model IV), as indicated by the PCV, 10.5% of the variation in the survival time across communities was explained by both individual and community-level factors. Including both individual- and community-level factors reduced the unexplained heterogeneity in the time to first ANC visit between communities from MAF of 2.70 2.31 in the null model to the MAF of 2.50 1.89 in the final model, which equals 0.42. This showed that the survival time to first ANC visit reduced by 58% when a woman moved from high risk to low-risk neighborhoods Table 3.

Table 3 Measures of variation and model fit statistics for time to first ANC visit among women in Ethiopia, 2023

	Null model	Model II	Model III	Model IV
Random effect result				
Variance	0.7686926	0.5209301	0.4975675	0.4451822
ICC (%)	18.9	13.7	13.1	11.9
PCV (%)	Reference	32.2	4.5	10.5
MHR	2.31	1.99	1.96	1.89
Model fit statistics				
-Log likelihood	-2552.5567	-2086.979	-2494.9995	-2011.4754
AIC	5111.113	4203.958	5019.999	4076.951
DIC	5105.1134	4173.958	4989.999	4022.9508

Based on the AIC and DIC, Multilevel mixed-effects Weibull survival model (Model IV) was found the best model to fit the data with a minimum AIC and DIC values of 4076.951 and 4022.951, respectively Supplementary Table 1.

The survival plot in **Error! Reference source not found.** shows that the survivor function for rural women is above the survivor function for urban women. This implies that rural women have a greater probability of not initiating an ANC visit at earlier gestational age (Figure 1 Mixed-effects AFT Weibull regression of time to first ANC visit by place of residence).

(Figure 1 Mixed-effects AFT Weibull regression of time to first ANC visit by place of residence)

Interpretation of the multilevel Weibull model results

The results of multivariable multilevel parametric Weibull survival analysis of predictors of the survival time to first ANC visit is provided in Table 4. The acceleration factor for mothers who gave birth in Home compared to those delivered in Health facility was 1.34 (95% CI: 1.20, 1.49). This shows that Home delivered mothers have a 34% longer survival time to start a first ANC visit. Similarly, Grand multiparous women have a 19% longer time to start ANC early in the first trimester than primipara women. The acceleration factor for Grand multiparous women was 1.19 (95% CI: 1.02, 1.39).

Media access was found to be a significant predictor of the survival time to first ANC visit. The acceleration factor for women who have access to media was 0.90 (95% CI: 0.81, 0.99). This shows that women who have media access had a 10% shorter time to start ANC in the first trimester of pregnancy than women who have no media access. Similarly, women whose last birth was caesarean section had a 28% shorter time to initiate ANC early in the first trimester as compared to those who delivered vaginally (AFT=0.72, 95% CI: 0.63, 0.82) Table 4.

Women with higher education had a 29% shortened time to start first ANC visit than those who were not educated. The acceleration factor for women with higher education was 0.71 (95% CI: 0.59, 0.85). Moreover, those with primary education had an 11% shortened time to commence ANC visit early in the first trimester of pregnancy (AFT=0.89, 95% CI: 0.80, 0.98). The acceleration factor for mothers who were formerly in union was 1.43 (95% CI: 1.14, 1.78). This indicates that mothers who were formerly in union commenced ANC visit later than mothers who were currently in union at 5% level of significance Table 4.

Place of residence was found to be a significant predictor of the survival time to first ANC visit. The acceleration factor for women who were rural residents was 1.20 (95% CI: 1.01, 1.43). This shows that women from a rural residency had 1.20 times prolonged time to start their first ANC visit early in pregnancy relative to those who were from an urban residency. Administrative region was also a significant predictor of time to first ANC visit Table 4.

Table 4 Mixed-effects Weibull AFT survival regression of time to first ANC visit among women in Ethiopia, 2023

Variables	Null Model	Model II	Model III	Model IV
Place of last birth				
Facility		1		1
Home		1.36(1.22, 1.51)***		1.34(1.20, 1.49)***
Parity				
1		1		1
Multipara		1.05(0.95, 1.17)		1.06(0.96, 1.18)
Grand multipara		1.23(1.06, 1.43)**		1.19(1.02, 1.39)*
Media Access				
No		1		1
Yes		0.82(0.75, 0.90)***		0.90(0.81, 0.99)*

Last birth		
Vaginal	1	1
C/S	0.71(0.62, 0.82)***	0.72(0.63, 0.82)***
Mothers education		
No education	1	1
Primary	0.90(0.81, 0.99)*	0.89(0.80, 0.98)*
Secondary	1.04(0.89, 1.21)	1.01(0.87, 1.18)
Higher	0.68(0.57, 0.81)***	0.71(0.59, 0.85)***
Marital status		
Currently in union	1	1
Formerly in union	1.42(1.13, 1.77)**	1.43(1.14, 1.78)**
Never in union	1.03(0.65, 1.65)	1.05(0.66, 1.68)
Maternal age		
Below 20 years	1	1
20-34 years	0.90(0.74, 1.08)	0.87(0.72, 1.07)
35 or more years	1.10(0.90, 1.34)	1.08(0.85, 1.37)
Community ANC		
Low	1	1
High	0.75(0.66, 0.84)***	0.92(0.78, 1.07)
Residency		
Urban	1	1
Rural	1.33(1.18, 1.50)***	1.20(1.01, 1.43)*
Region		
Addis Ababa	1	1
Tigray	1.24(0.94, 1.64)	1.06(0.80, 1.43)
Afar	1.13(0.68, 1.90)	0.92(0.61, 1.41)
Amhara	1.27(0.99, 1.62)	0.96(0.73, 1.26)
Oromia	1.45(1.14, 1.84)**	1.13(0.86, 1.48)
Somalia	1.51(1.03, 2.22)*	1.14(0.76, 1.70)
Benishangul	1.37(0.82, 2.29)	1.18(0.77, 1.83)
SNNPR	1.66(1.29, 2.14)***	1.50(1.18, 2.01)**

Gambella	1.36(0.64, 2.90)	1.32(0.71, 2.46)
Harari	0.83(0.36, 1.89)	0.83(0.46, 1.48)
Dire Dawa	0.89(0.50, 1.60)	0.83(0.54, 1.28)

* Statistically significant at P-value< 0.05; ** statistically significant at P-value p < 0.01; *** statistically significant at P-value < 0.001, 1 = Reference category

Discussion

Timely initiation of ANC visit in Ethiopia was found to be 42.7% (95% CI: 41.0 – 44.6). This result is higher than the previous study conducted in Ethiopia that reported timely initiation of ANC visit of 38.6%(34). This finding is significantly higher than studies done in Benin, Kenya, and Nigeria(35)(36)(37), but lower compared to a study from Ghana, where first trimester initiation of ANC visit was reported to be as high as 57%(27).

The mean survival time of pregnant women to initiate the first ANC visit was 6.8 months. This finding was slightly higher than a study done in Nigeria in which the reported median survival time to first ANC visit was 6 months(37). This finding is higher when compared to the recent findings of average of 3.4 gestational months before initiation of ANC visit in Ghana(27).However, late initiation of ANC visit has been previously reported in Ethiopia with a median survival time of 7 months(34).

Women who had higher education, and who had primary education had a 29%, and 11% shortened time to start first ANC visit than those with no education. This finding is in agreement with findings of previous studies(38)(9). A retrospective study from Ethiopia revealed that early initiation of ANC increases as the women's level of education increases compared to women who have no formal education(9). A multi-country analysis of DHS in SSA found that the odd of timely initiation of ANC was higher in mothers who had higher level of education compared to

women who had no formal education(8).A study from Nigeria revealed that women with higher education were more likely to start first ANC visit early compared to uneducated women(37). Similarly, in Nepal, women with higher level education were significantly more likelyto initiate ANC early compared to women who had no education(38).

The possible explanation could be due to women with a secondary and above level of education might be more likely to be employed, financially independent, and knowledgeable on the necessity of having antenatal care follow-up during pregnancy, as a result, they might be more likely to realize the importance of early booking their first ANC visit timely(39).Additionally, uneducated women might have limited understanding of ANC services and their importance to their unborn fetus wellbeing and ensure safe delivery(9). It is because education will change the knowledge when to start ANC awareness of the mothers to start and follow the health services appropriately (16).

This study indicated that women who were formerly in union commenced ANC visit later than mothers who were currently in union at 5% level of significance. This evidence is in line with the studies done in South Africa and Rwanda in which currently married women were more likely to initiate ANC in the first trimester of pregnancy(24)(26). This might be due to the fear of social rumors, and hence, lack of confidence in seeking care for unborn child whose father is not formal or in doubt. Another possible explanation can be the work load hanged on her shoulder only to improve the life of her unborn child and herself too. Furthermore, they might not know whether they are pregnant timely, and even if they knew it early, they may not be interested with the pregnancy, they may be careless for the conception and fail to book early.

The findings of this study indicate that having the father of the child present in the woman's life during pregnancy shortens the time to first ANC attendance and highlight a need to involve male partners in reproductive health issues including family planning and maternal health care.

Grand multiparous women had a 19% longer time to start ANC early in the first trimester than primipara women. In Nigeria, women with one birth were 1.90 times more likely to initiate ANC in the first trimester compared to women with five and above births(20). In Malawi, women with more than five births were 12% less likely to access ANC services in their first trimester of pregnancy(40). A population study from Ethiopia showed that multi-parous women had higher odds of delayed initiation of ANC visit when compared to the primi-parous women(23). Another survival study from Ethiopia found that women with four and above births had a 20% hazard of delayed initiation of ANC follow up as compared to one parity(9).

This might be attributable to high parity women's increased confidence from previous pregnancy and childbirth experience. Additionally, high parity women might have poor prior experience with the health system, and constraints of time and resources to access ANC services early(36).

This study also showed that women from a rural residency had a prolonged time to start their first ANC visit relative to those who were from an urban residency. In SSA, women residing in the rural area were less likely to initiate ANC timely within 12 weeks of gestation(8).In Nigeria, women in urban areas were more likely to make the first ANC visit early in the first trimester of pregnancy(37).A study in Ethiopia using the 2016 EDHS data set indicated that rural women have prolonged time-to start first ANC visit than urban women(19). In Ethiopia, women from rural residency were 18% less likely to attained ANC early in pregnancy than urban counter

parts(9). Another similar study in Ethiopia showed that rural women were 59% less likely to start their first ANC visit within the first trimester than urban counterparts(10).

This study showed that women whose last birth was in Home had a 34% longer survival time to start a first ANC visit compared to those whose last birth was in Health facility. This result is supported with the finding reported from Mandera County in Kenya in which women who utilized skilled delivery service were more likely to have used ANC services more than those who had not utilized the service(36).

Media access was found to be a significant predictor of the survival time to first ANC visit. Women who have media access had a 10% shorter time to start ANC in the first trimester of pregnancy than women who have no media access. This is similar to findings in(19)(9), suggesting that women who have access to media were more likely to initiate ANC at an earlier gestational age. Access to media is associated with increased knowledge about the benefit of using maternal health services which compels women to better use antenatal care services.

Women whose last birth was caesarean section had a 28% shorter time to start first ANC than those who gave their last birth vaginally. This finding is supported with previous similar studies(41)(36)(42). A previous study done in Uganda showed that women who gave birth by caesarean section were more likely to initiate the first ANC visit in the first trimester of pregnancy(41). In Kenya, women who had complications during last pregnancy were two times more likely to utilize ANC than those who had no complication(36). A study from Mekelle, Ethiopia revealed that women with history of still birth, and obstetric problem in the current pregnancy were more likely to book ANC early in pregnancy(42).

Study limitations and strengths

This study used secondary data that were collected cross-sectionally through self-reported interviews, which are prone to recall errors and social desirability bias. In addition, some factors that are probably crucial in determining the timing of the first ANC visit were not available for consideration in the existing EMDHS data, such as the standard of ANC provided and women's perceptions of the ANC.Despite these drawbacks, the current study used a large sample from nationally representative survey data in Ethiopia. The study's findings were representative of all regions. The study also attempted to analyze community-level variables related to the survival time to first ANC visit. Another advantage of the study is its sophisticated statistical design, which allows for greater reliability of the results and allows for the control of confounding factors.

Conclusion

The study indicated that women in the study area sought their initial antenatal care at a health facility far later than the WHO recommended.The independent predictors, women's education level, media exposure, and prior cesarean delivery made early ANC initiation possible.Increasing parity, being previously in a union, having a home birth, and living in a rural area were the impediments for early ANC initiation.

It's crucial to provide health education with a focus on empowering expectant mothers to timely activate prenatal care, especially for those who give birth at home and for those who reside in remote areas. To do this, healthcare practitioners should work in conjunction with community health workers.Expanding health education through the use of media should also be a part of initiatives to boost the timely initiation of antenatal care utilization.

This study also has the implication that policies aiming to decrease pregnancy-related preventable morbidity and mortality through the use of timely antenatal care must prioritize educating and empowering women.

Abbreviations and Acronyms

AAF: Adjusted Acceleration Factor; AFT: Accelerated Failure Time; ANC: Antenatal Care; CI: Confidence Interval; DHS: Demographic and Health Survey; EMDHS: Ethiopian Mini Demographic and Health Survey; ICC: Intraclass Correlation Coefficient; MAF: Median Acceleration Factor; PCV: Proportional Change in Variance; PNC: Postnatal Care.

Declarations

Ethics approval and consent to participate

Ethics review and participant consent were not required for this study because it used secondary data analysis of publicly available survey data from the Measure DHS program. A written letter of permission was secured from the IRB of Demographic and Health Survey (DHS) program data archivists to download and use the data for this study from https://www.dhsprogram.com. This study was performed in line with the principles of the Declaration of Helsinki. The DHS data were kept confidential, and any identifying information was removed. The data was only used for this particular, authorized research project, and it would not be shared with any researchers.

Consent for publication

Not applicable

Availability of data and materials

The data sets recoded and analyzed during this study are available in the Measure DHS program repository to all registered users (https://www.dhsprogram. com/data/dataset_admin)

Competing interests

The authors declare that they have no competing interests.

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Author's contributions

HZA conceived the study, participated in its design and coordination, initiated the research, carried out the statistical analysis, interpreted the results, and wrote the final manuscript, critically reviewing it. BTO and MA participated in the study's design, guided the statistical analysis, and critically reviewed the manuscript. DG, HI and TG were involved in principal supervision, participated in the study's design and coordination, edited the manuscript, and critically reviewed the manuscript. The authors have read and approved the final manuscript.

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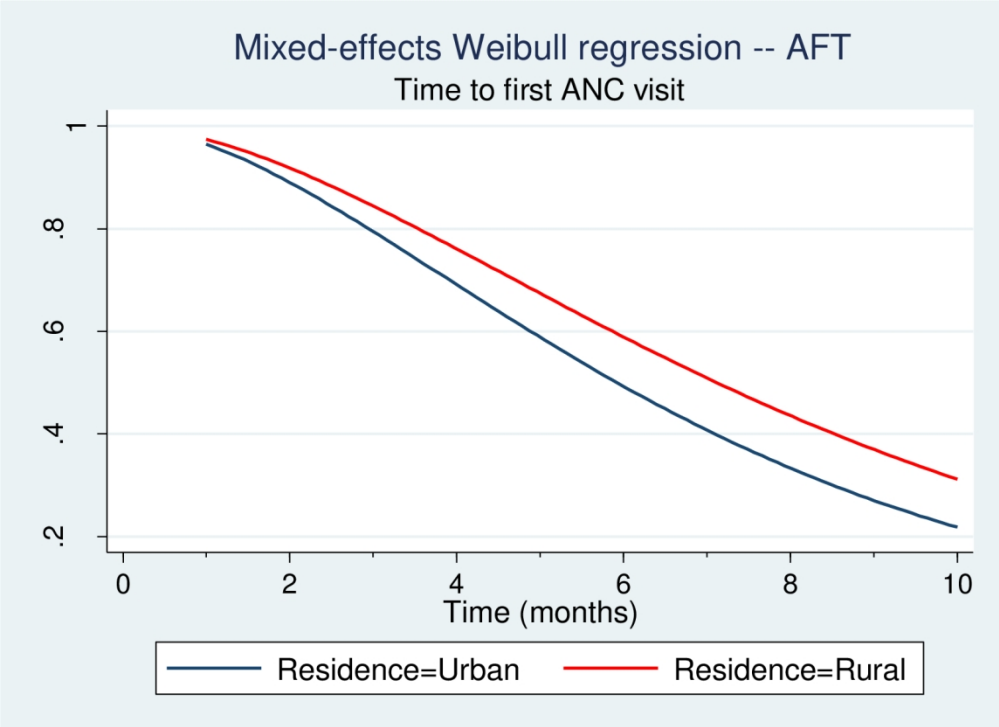

Figure 1 Mixed-effects AFT Weibull regression of time to first ANC visit by place of residence

139x101mm (300 x 300 DPI)

Supplementary Table 1 Comparison of Mixed-effects AFT model with different baseline distributions

Model	Parameters	-Log Likelihood value (Full)	DIC value	AIC value	BIC
Exponential	26	-2991.507	5983.014	6035.014	6186.615
Weibull	27	-2011.4754	4022.951	4076.951	4234.383
Log-normal	27	-2769.9096	5539.819	5593.819	5751.251
Log-logistic	27	-2797.6489	5595.298	5649.298	5806.73
Gamma	27	-2817.812	5635.623	5689.623	5847.055

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Time to initiation of antenatal care and its predictors among pregnant women in Ethiopia: Multilevel Mixed-effects Acceleration Failure Time model

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Time to initiation of antenatal care and its predictors among pregnant women in Ethiopia: Multilevel Mixed-effects Acceleration Failure Time model

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Abstract

Objective: To assess the time-to-initiation of antenatal care and its predictors among pregnant women in Ethiopia.

Design: Retrospective follow-up study using secondary data from the 2019 Ethiopian mini demographic and health survey.

Setting and participants: 2933 women aged 15 to 49 who had ANC visit during their current or most recent pregnancy within the five years prior to the survey were included in this study. Women who attended prenatal appointments but whose gestational age was unknown at the first prenatal visit were excluded from the study.

Outcome measures: Participants were interviewed to respond the gestational age in months at which they made the first antenatal care visit. Multivariable Mixed-effects survival regression was fitted to identify factors associated with the time-to-initiation of ANC.

Results: In this study, the estimated mean survival time of pregnant women to initiate the first ANC visit in Ethiopia was found to be 6.8 months (95% CI: 6.68, 6.95). Women whose last birth was a caesarean section (AAF = 0.75, 95% CI: 0.61, 0.93), and women with higher education (AAF = 0.69; 95% CI: 0.50, 0.95) had a shorter time to initiate ANC early in the first trimester of pregnancy. However, being grand multiparous (AAF = 1.31; 95% CI: 1.05, 1.63), being previously in a union (AAF = 1.47; 95% CI: 1.07, 2.00), having a home birth (AFT = 1.35; 95% CI: 1.13, 1.61), and living in a rural area (AAF = 1.25; 95% CI: 1.03, 1.52) were the impediments for early ANC initiation.

Conclusion: Women in this study area sought their initial antenatal care far later than the WHO recommended. Therefore, healthcare providers should collaborate with community health workers to provide home-based care in order to encourage prompt ANC among hard-to-reach populations, such as rural residents and those giving birth at home.

Strength and limitations of this study

- This study used a large, nationally representative sample from Ethiopian survey data.
- This study evaluated community- and individual-level factors related to the survival time to initiation of ANC visit using a robust model.
- Many factors that could affect the timing of the first ANC visit were not taken into account in this study because they were not present in the original data.
- Social desirability bias is likely to arise because the data were collected through self-reported interviews with participants.

Introduction

A healthy pregnancy for both mother and child, a smooth transition to a happy labor and delivery experience, and successful parenthood are all aspects of the positive pregnancy experience that women want and need.(1) However, the morbidity and mortality rates associated with pregnancy that are preventable are still too high at the outset of the Sustainable Development Goals (SDG) period. In order to improve the pregnancy's outcome, antenatal care (ANC) is a crucial time for health promotion, screening, and disease prevention.(2) For multidisciplinary care providers, the early antenatal care visit is the best opportunity to intervene with health promotion activities and establish a baseline knowledge of the pregnant woman's pre-existing medical conditions.(3)

Early detection of modifiable risk factors and pre-existing conditions is made possible by timely prenatal care initiation, which is defined as the first antenatal contact taking place during the first trimester of pregnancy.(4) The 2016 World Health Organization (WHO) recommendation also suggests early beginning of ANC within the first 12 weeks of gestation.(2) Women with early ANC initiation are more likely to have sufficient amount of antenatal care contacts.(5) A study from low and middle income countries have shown that receiving early ANC was associated with a higher likelihood of having eight plus ANC visit.(6) According to a Pakistani study, women who had their first ANC checkup within three months of being pregnant were more likely to obtain WHO-recommended services during their pregnancy, indicating that the timing of the checkup is a strong predictor of the content of services.(7)

There has been a significant improvement in the estimated global coverage of early prenatal care visits, going from 40.9% in 1990 to 84.8% in 2013, or a 43.3% increase.(4) The Estimated

coverage of early prenatal care visits in low-income countries (LMICs) in 2013 was 24 percent, compared to 81 percent in high-income countries.(4) Data from these nations' Demographic Health Surveys (DHS) from 2012 to 2018 show that this percentage has climbed to 44.3%.(5) Yet, this shows that the rate of early initiation of ANC in the LMICs is very far from the optimal level.

A woman dies every two minutes due to pregnancy or childbirth according to United Nations (UN) estimates.(8) The poorest nations and those experiencing conflict continue to have the highest rates of maternal fatalities. With 3.6% of all maternal deaths worldwide in 2020, Ethiopia had the fourth-highest estimated number of maternal deaths, behind Democratic Republic of the Congo, Nigeria, and India.(8) Timely ANC initiation is essential to lowering maternal morbidity and mortality in countries with high rates of maternal morbidity and mortality.(9)

The magnitude timely initiation of ANC visit in Sub-Saharan Africa was 38.0%, ranging from 14.5% in Mozambique to 68.6% in Liberia.(10) In Ethiopia, being one of the SSA countries, the problem is even worse. The median time to antenatal care initiation in the country was found to be 5 months.(11) The result from 2016 Ethiopian Demographic Health Survey (EDHS) revealed only 20% of pregnant women in Ethiopia start their ANC during the first trimester of their pregnancy.(12) Other studies in the country reported varying magnitude of early initiation of ANC; the proportion was found to be 46.8% in Bahirdar,(13) 21.71% in southern Ethiopia,(14) 40.6% in Debre Markos,(15) 39.5% in Tselemt district of Tigray Region,(16) 27.5% in Axum,(17) 28.8% in Ilu-Ababor,(18) 34% in Bench-Sheko zone.(19)

Predictors of timing of first antenatal care follow up from different literatures were residence,(10,12,20) household wealth,(10,21) educational status of the women,(10,11,17) media exposure,(10,11,20) occupation of the women,(22–24) parity,(11,25,26) husband education,(20,21) husband occupation,(20) distance from health facility,(10,26) and maternal age.(10,21,27)

Despite various studies on identifying risk factors for time to first ANC follow-up were conducted in Ethiopia, only few studies found to be representative at the national level. Furthermore, almost all of the studies failed to consider community-level factors for time to initiation of ANC in Ethiopia. Updated and nationally representative information is very crucial

for policy makers and other concerned bodies to improve the level of early antenatal care initiation. Respecting women's rights and providing them with early prenatal care is the first step in a lifetime of care that will improve both mother and child's health.(3) Therefore, this study undertook a retrospective analysis based on the 2019 Ethiopian Mini Demographic and Health survey (EMDHS) data set, to identify time-to-initiation of ANC and its predictors in Ethiopia.

Methods

Study design and area

This study undertook a retrospective analysis based on the 2019 Ethiopian Mini Demographic and Health survey (EMDHS) data set. Ethiopia is located in the Horn of Africa and shares a border with Eritrea, Djibouti, Somalia, Sudan, South Sudan, and Kenya. It is the second most populous nation in Africa, with over 110 million populations.(28) Based on the 2021 World Bank reports Ethiopia had a gross national income per capital of US$ 940.(29)

Data source and sampling procedure

Ethiopian Mini Demographic and Health Survey (EMDHS) 2019 data was used in this investigation. Once the Measure DHS website (http://www.measuredhs.com) was contacted online with an explanation of the study's purpose, the data were provided. The EMDHS 2019's under-five children's file (KR) and individual women's file contained the variables that were used in this investigation. The 2019 EMDHS sample was stratified and selected in two stages, and interviews were conducted face-to-face with permanent residents and visitors who stayed in the residences the day before the survey. The 2019 EMDHS sampling frame is a composite of all census enumeration areas (EAs) created for the upcoming 2019 Ethiopia Population and Housing Census (PHC) conducted by the Central Statistical Agency (CSA). The census frame includes the complete list of 149,093 EAs created for the 2019 PHC. An EA is a geographical area with an average of 131 households. The sampling frame includes data on the EA's location, type of residence (urban or rural), and the estimated number of residential households.(30)

Study population

All women aged 15 to 49 who had ANC during their current or most recent pregnancy within the five years prior to the survey were included in this study. Women who attended prenatal appointments but whose gestational age was unknown at the first prenatal visit were excluded

from the study. A total of 2933 women aged 15 to 49 who had ANC visit during their current or most recent pregnancy were therefore analyzed in this study.

Study variables

Outcome of interest

The dependent variable is time-to-first ANC receipt among pregnant women which is measured in months. The event of interest considered as success (event = 1) if women had antenatal care in the first trimester of pregnancy and otherwise censored (censored = 0).

Independent variable

Individual level factors were women education level, household wealth index, birth interval, number of antenatal care visit, age of the women, media exposure and marital status.

Community level factors were residence, region, community educational status, community ANC coverage and community poverty. The EMDHS did not collect data that can directly describe the clusters' characteristics except the place of residence and region. Therefore, other common community-level data were generated by aggregating the individual characteristics with our interest in a cluster. The aggregates were computed using the proportion of a given variables' subcategory we were concerned on in a given cluster. Since the aggregate value for all generated variable was not normally distributed. It was categorized into groups based on the national median values.

The proportion of a given variable's subcategory in a particular cluster was used to construct the aggregates. The aggregate value for all newly created variables had a non-normal distribution, so it was split into two categories (low and high proportions) based on their median values. Community women's education is measured as the proportion of women in the cluster with secondary or higher education. Community-level poverty was defined as the proportion of women in the bottom 2 household wealth quantiles (poorer and poorest) in the cluster. The percentage of women in a cluster who utilize ANC was used to define community ANC utilization. Place of residency and region were used as they were categorized in the EMDHS data set.

Operational definition

Exposure to mass media: a frequency of listening to the radio and watching television were

considered exposure to mass media in this study by excluding exposure to magazines and newspapers. So, women exposed to either television or radio at least once per week considered exposed, if not exposed at all, taken as not exposed.

Community women education: Was defined as the proportion of mother's who attended primary/secondary/ higher education within the cluster. The aggregate of individual mother's primary/secondary/higher educational attainment can show the overall educational status of women within the cluster. There were two categories for this variable with reference to the national median value: higher proportion of mother's who attended primary/secondary/higher education and lower proportion of mother's who attended primary/secondary/higher education within the cluster.

Antenatal care utilization: was defined as mothers who had at least four antenatal care visit.(2)

Community antenatal coverage: The proportion of women in the clusters who had four and above antenatal care (ANC) from a skilled provider during the pregnancy of last delivery.

Community poverty status: It is defined as the proportion of poor or poorest mothers within the cluster. Within the cluster proportion of poor or poorest were aggregated and show over all poverty status within the cluster.

Data Quality Control and Assurance

The data sets for the original work were collected by face-to-face interviewing women using structured questionnaires that met the eligibility criteria. The woman's questionnaire, the household questionnaire, and the Health Facility Questionnaire were employed to gather essential information. After the questionnaires were finalized in English, they were translated into Amarigna, Tigrigna, and Afaan Oromo. In addition to this, the gathered data was back-translated into English to keep consistency. The quality of the dataset has maintained by testing its completeness. Moreover, the quality of the original data set was maintained by giving training to interviewers, and interviewers used tablet computers to record responses during the interviews.

For this study, the data were weighted using sampling weight before any statistical analysis to restore the representativeness of the data and to get a reliable estimate and standard error. The weighted results from the analysis were reported in the study. Multicollinearity between independent variables was checked using Variance Inflation Factor (VIF) and the mean VIF was 2.11. The proportional hazards (PH) assumption was tested using Scaled Schoenfeld residuals

and found to be unsatisfied, with a global test value of 0.0001. Multicollinearity between independent variables was checked using Variance Inflation Factor (VIF) and the mean VIF was 2.11. The data was also assessed for an interaction factor.

Data Management and Analysis

STATA version 14 software was used for cleaning, recoding, and analyzing the data. Descriptive statistics were applied using frequencies and percentages. Estimation of survival probability was done by using the Kaplan Meier survival curve. Survival curves were compared by log-rank test. Univariable survival regression was fitted for explanatory variables and those having p-value ≤0.25 level of significance were considered for the multivariable analysis. Then, the study applied a stepwise backward variable selection procedure to obtain the final reduced model. The proportional hazards (PH) assumption was tested using Scaled Schoenfeld residuals and found to be unsatisfied, with a global test value of 0.0001. Finally, a multivariable mixed-effects parametric Weibull distribution survival regression model was fitted. Adjusted Acceleration Factor (AAF) or Time ratio with its 95% confidence interval (CI) was applied, and covariates with a P-value <0.05 in the multivariable analysis were considered determinants of the survival time to first ANC visit.

Survival analysis

Survival analysis deals with the analysis of survival data, which is used to measure the time to an event of interest, such as death or failure.(31) The Cox proportional hazard model is one of the most widely used regression model types in survival analysis. The Cox model estimates the hazard ratio, which is always a nonnegative value. The primary attribute of the Cox model is its reliance on the proportional hazards assumption, which states that "coefficients of the hazard function must remain constant across time for a given covariate".(31)

Parametric acceleration failure time model

An acceleration failure time model (AFT) is a parametric model in the statistical field of survival analysis that offers an alternative to the often used PH models. The primary distinction between Cox model and AFT is that the baseline hazard function is supposed to follow a specific distribution in AFT models. Covariate multiplies the hazard by a constant in a PH model, while it accelerates or decelerates a failure status's life cycle (initiation, discontinuation, disease, death or recovery) by a constant in an AFT model.(32)

Accelerated Failure Time (AFT) model is a model used for adjusting survivor functions for the effects of covariates. In the AFT parameterization, the natural logarithm of the survival time, log *t*, is expressed as a linear function of the covariates:(31)

$$\log(t_j) = X_j\beta + Z_j u_j + v_j \quad \ldots\ldots 1$$

for j = 1, . . . , M clusters with cluster j consisting of i = 1, . . . , nj observations. The vector x_{ji} contains the covariates for the fixed effects, with regression coefficients (fixed effect) β. The vector z_{ji} contains the covariates corresponding to the random effects uj. v*ji* are observation-level errors with density ϕ(·). The distributional form of the error term determines the regression model. Five regression models are implemented in mestreg using the AFT parameterization: exponential, gamma, loglogistic, lognormal, and Weibull. Therefore, this study fitted a random-effects Weibull model with normally distributed random effects. This model can be viewed as a shared frailty model with lognormal frailty.

Mixed-effects parametric survival analysis

The EMDHS used a multistage cluster sampling technique, whereby data were hierarchical (i.e., pregnant women were nested within households, and households were nested within clusters). Considering the hierarchical nature of EMDHS data, pregnant women who lived within the same cluster may have had similar characteristics compared to those who reside in other clusters of the country. Therefore, a two-stage multivariable mixed-effects parametric survival regression analysis was employed to estimate the effects of individual and community level predictors on the survival time to first ANC visit. Mixed-effects survival models contain both fixed effects and random effects.

Four models were fitted to identify community and individual level factors associated with infant death. The first model (Model 1 or empty model) contained no explanatory variables. The second model (Model 2) considered only the individual-level variables in order to examine the individual-level effect. The third model (Model 3) considered only the community-level variables in order to examine the effect of community-level factors on infant death, independent of other factors. The fourth model (Model 4) is the full model that incorporated all individual and community-level variables into the multilevel analysis.

The fixed effect sizes of individual and community-level determinants of the survival time to first ANC visit were expressed as AAFs with 95% CI. The P-value <0.05 has been considered as statistically significant. Additionally, the measure of variance (random effects) was reported in

terms of the intraclass correlation coefficient (ICC), median acceleration factor (MAF), and proportional change in variance (PCV). Model fitness was checked using Akaike Information Criteria (AIC) and Deviance Information Criteria (DIC). The lowest AIC and DIC values declare the best fit model.(31)

Patient and public involvement

Women in their reproductive years who had ANC during their current or most recent pregnancy within the five years prior to the survey took part in this study and contributed vital data. However, they never participated in conducting the study, designing the protocol or instruments used to gather the study's data, reporting the findings, or distributing them.

Result

Descriptive statistics

Weighted samples of 2924 women were followed for a minimum of 1 and a maximum of 10 months with an average follow up time of 4 months. In this study, timely initiation of ANC visit in Ethiopia was found to be 42.7% (95% CI: 41.0 – 44.6). The estimated mean (restricted) survival time of pregnant women to initiate the first ANC visit was 6.8 months (95% CI: 6.68, 6.95). The overall incidence rate was approximately 11 per 100 person month of observation. Majority 2755 (94.2%) of women were currently married or inunion, and of these 1030 (37.4%) had initiated ANC visit early in the first trimester of pregnancy. Regarding women education, 1283 (43.9%) women had no education, and among these 404(31.5%) initiated their ANC visit timely. Access to media was reported by 1259(43.1%) of whom 582(46.2%) had started ANC visit within 12 weeks of pregnancy. More than half 114(58.5%) of women who gave birth by C/S started their first ANC visit within the first trimester (Table 1 Summary of individual and community level factors of time to ANC initiation among study participants (2924), 2022).

Most 2052(70.2%) of the women were rural residents, and among these only 647(31.5%) women initiated ANC visit within the recommended time. The proportion of women starting first ANC visit within the first trimester was higher in Harari (66.7%), Dire Dawa (66.7%) and Addis Ababa (65%), whereas lower in the SNNPR (28.8%), Oromia (33.2%) and Somali (33.3%) regional states. More than half 1577(53.9) of the women were from a community with a low

poor proportion of whom 740(46.9%) commenced their first ANC visit in the first three months of pregnancy. Moreover, 353(26.2%) women from a community with a high poor proportion commenced their first ANC visit timely (Table 1 Summary of individual and community level factors of time to ANC initiation among study participants (2924), 2022).

Comparison of the different covariate in terms of survival time to first ANC visit

Kaplan Meier graphs are generated to observe the difference in the survival time to first ANC visit of women for different categorical variables. The log-rank test was carried out to validate the difference between the groups of each categorical variable. The log-rank test result (Table 2) shows that there is statistically significant difference in the survival experience of groups among women education level ($p < 0.0001$), wealth index ($p < 0.0001$), delivery place ($p < 0.0001$), parity ($p < 0.0001$), media access ($p < 0.0001$), region ($p < 0.0001$), women age ($p < 0.001$) and Marital status ($p < 0.2$) (Table 2 Comparison of survival time of individual and community level factors of time to ANC initiation among study participants (2924), 2022).

Random effects and model comparison

As the multilevel mixed-effects Weibull survival regression analysis results described in Table 3, Model I revealed statistically significant variation in the survival time to first ANC visit of women across communities. Nearly One fifth of the variation in the survival time is attributed to community-level factors (ICC = 18.9%). After adjusting the model for individual-level factors (Model II), about 32.4% of the variation in the accelerations of survival time was attributed to the individual level factors (PCV = 32.4%), and 13.6% of the variance in the survival time was attributed to community-level factors (ICC = 13.6%). Model III, which was adjusted for community-level factors, revealed that the community level factors explained 4.12% of the variability in the accelerations of survival time to first ANC visit of women (PCV = 4.12%), and 13.1% of the variation among the clusters was attributed to community-level factors (ICC =

13.1%) (Table 3 Measures of variation and model fit statistics for time to first ANC visit among women in Ethiopia, 2023).

The final best-fit model (model IV) was adjusted for both individual and community-level factors simultaneously. In this final model (model IV), as indicated by the PCV, 16.1% of the variation in the survival time across communities was explained by both individual and community-level factors. Including both individual- and community-level factors reduced the unexplained heterogeneity in the time to first ANC visit between communities from MAF of 2.31 in the null model to the MAF of 1.85 in the final model, which equals 0.46. This showed that the survival time to first ANC visit reduced by 54% when a woman moved from high risk to low-risk neighborhoods (Table 3 Measures of variation and model fit statistics for time to first ANC visit among women in Ethiopia, 2023).

Based on the AIC and DIC, Multilevel mixed-effects Weibull survival model (Model IV) was found the best model to fit the data with a minimum AIC and DIC values of 4075.578 and 4021.578, respectively ""Supplemental Table 1"".

The survival plot in **Error! Reference source not found.** shows that the survivor function for rural women is above the survivor function for urban women. This implies that rural women have a greater probability of not initiating an ANC visit at earlier gestational age (**Error! Reference source not found.**).

Interpretation of the multilevel Weibull model results

The results of multivariable multilevel parametric Weibull survival analysis of predictors of the survival time to first ANC visit is provided in Table 4 (Table 4 Mixed-effects Weibull AFT survival regression of time to first ANC visit among women in Ethiopia, 2023).

The acceleration factor for mothers who gave birth in Home compared to those delivered in Health facility was 1.35 (95% CI: 1.13, 1.61). This shows that Home delivered mothers have a 35% longer survival time to start a first ANC visit. Similarly, Grand multiparous women have a 31% longer time to start ANC early in the first trimester than primipara women. The acceleration factor for Grand multiparous women was 1.31 (95% CI: 1.05, 1.63).

Women with higher education had a 31% shortened time to start first ANC visit than those who were not educated. The acceleration factor for women with higher education was 0.69 (95% CI: 0.50, 0.95). Similarly, women whose last birth was caesarean section had a 25% shorter time to initiate ANC early in the first trimester as compared to those who delivered vaginally (AAF = 0.75, 95% CI: 0.61, 0.93) (Table 4 Mixed-effects Weibull AFT survival regression of time to first ANC visit among women in Ethiopia, 2023).

The acceleration factor for mothers who were formerly in union was 1.47 (95% CI: 1.07, 2.00). This indicates that mothers who were formerly in union commenced ANC visit later than mothers who were currently in union at 5% level of significance (Table 4 Mixed-effects Weibull AFT survival regression of time to first ANC visit among women in Ethiopia, 2023).

Place of residence was found to be a significant predictor of the survival time to first ANC visit. The acceleration factor for women who were rural residents was 1.25 (95% CI: 1.03, 1.52). This shows that women from a rural residency had 1.25 times prolonged time to start their first ANC visit early in pregnancy relative to those who were from an urban residency. Administrative region was also a significant predictor of time to first ANC visit (Table 4 Mixed-effects Weibull AFT survival regression of time to first ANC visit among women in Ethiopia, 2023).

Discussion

In this study, Ethiopian pregnant women's time-to-initiation of ANC and its predictors were evaluated. Pregnant women's mean survival time to schedule their first ANC check was thus 6.8 months (95% CI: 6.68, 6.95). Furthermore, the time-to-initiation of ANC was significantly associated with factors such as women's educational attainment, prior cesarean birth, parity, marital status, place of delivery, place of residency, and region of residency.

The mean survival time of pregnant women to initiate ANC visit in this study was significantly higher than a study done in India in which the reported median survival time to first ANC visit was 4 months. (33) The finding of this study is also slightly higher than the study finding from Nigeria in which the median survival time for the first ANC checkup was found to be 6 months.(34) Moreover, this finding is higher when compared to the recent findings of average of

3.4 gestational months before initiation of ANC visit in Ghana.(27) However, late initiation of ANC visit has been previously reported in Ethiopia with a median survival time of 7 months.(35)

Timely initiation of ANC visit within the first three months of pregnancy in Ethiopia was found to be 42.7% (95% CI: 41.0, 44.6). This finding is lower than the study conducted in Pakistan which indicated that nearly half of women (48%) received ANC within 3 months of pregnancy.(7) This finding is significantly higher than studies done in Tanzania,(36) Benin,(37) Kenya,(38) and Nigeria,(34) but lower compared to a study from Ghana, where first trimester initiation of ANC visit was reported to be as high as 57%.(27) This result is higher than the previous study conducted in Ethiopia that reported timely initiation of ANC visit of 38.6%.(35)

Women who had higher education had a 31% shortened time to start first ANC visit than those with no formal education. This finding is in agreement with findings of previous studies. (11,33,39) A study conducted in India revealed that women with higher education had a 2.8 times shorter time to initiation of ANC in the first trimester of pregnancy compared to women having no formal education.(33) Similarly, in Nepal, women with higher level education were significantly more likely to initiate ANC early compared to women who had no education.(39) A multi-country analysis of DHS in SSA found that the odd of timely initiation of ANC was higher in mothers who had higher level of education compared to women who had no formal education.(10) A study from Nigeria revealed that women with higher education were more likely to start first ANC visit early compared to uneducated women.(34) A retrospective study from Ethiopia revealed that early initiation of ANC increases as the women's level of education increases compared to women who have no formal education.(11)

The possible explanation could be due to women with a higher level of education might be more likely to be employed, financially independent, and knowledgeable on the necessity of having antenatal care follow-up during pregnancy, as a result, they might be more likely to realize the importance of early booking their first ANC visit timely.(40) Additionally, uneducated women might have limited understanding of ANC services and their importance to their unborn fetus wellbeing and ensure safe delivery.(11) It is because education will change the knowledge when to start ANC awareness of the mothers to start and follow the health services appropriately.(18)

This study indicated that women who were formerly in union commenced ANC visit later than mothers who were currently in union at 5% level of significance. The findings of this study indicate that having the father of the child present in the woman's life during pregnancy shortens the time to first ANC attendance and highlight a need to involve male partners in reproductive health issues including maternal health care and family planning. This evidence is in line with the studies done in South Africa(24) and Rwanda(26) in which currently married women were more likely to initiate ANC in the first trimester of pregnancy.

This might be due to the fear of social rumors, and hence, lack of confidence in seeking care for unborn child whose father is not formal or in doubt. Another possible explanation can be the work load hanged on her shoulder only to improve the life of her unborn child and herself too. Furthermore, they might not know whether they are pregnant timely, and even if they knew it early, they may not be interested with the pregnancy, they may be careless for the conception and fail to book early. Women with an unwanted (24) and mistimed pregnancies (41) have been show to receive late ANC.

Grand multiparous women had a 31% longer time to start ANC early in the first trimester than primipara women. This evidence is supported by prior studies.(11,33,41,42) A study finding from India has shown that women with birth order of 4 and above had a 16% prolonged time to initiation of ANC compared to Primipara women.(33) In Malawi, women with more than five births were 12% less likely to access ANC services in their first trimester of pregnancy.(42) In Nigeria, women with one birth were more likely to initiate ANC in the first trimester compared to women with five and above births.(21) In Kenya, women with four and above births were 1.75 times more likely to start their first antenatal care late in pregnancy during the second and third trimesters of pregnancy compared to the Primipara women.(41)

A survival study from Ethiopia found that women with four and above births had a 20% hazard of delayed initiation of ANC follow up as compared to one parity.(11) Another population study from Ethiopia showed that multi-parous women had higher odds of delayed initiation of ANC visit when compared to the primi-parous women.(23) This might be attributable to high parity women's increased confidence from previous pregnancy and childbirth experience. Additionally, high parity women might have poor prior experience with the health system, and constraints of time and resources to access ANC services early.(38)

This study also showed that women from a rural residency had a prolonged time to start their first ANC visit relative to those who were from an urban residency. In India, urban residents had a 49% probability of initiating ANC early in the first trimester of pregnancy compared to rural counterparts.(33) In SSA, women residing in the rural area were less likely to initiate ANC timely within 12 weeks of gestation.(10) In Nigeria, women in urban areas were more likely to make the first ANC visit early in the first trimester of pregnancy.(34) A study from Kenya showed that the odds of timely initiation of ANC in the first 3 months of pregnancy was higher in women living in urban areas compared to the rural counterparts.(41)

A study in Ethiopia using the 2016 EDHS data set indicated that rural women have prolonged time-to start first ANC visit than urban women.(20) In Ethiopia, women from rural residency were 18% less likely to attained ANC early in pregnancy than urban counter parts.(11) Another similar study in Ethiopia showed that rural women were 59% less likely to start their first ANC visit within the first trimester than urban counterparts.(12) This might be because urban women have easier access to transportation and social media, which help them easily, obtain information about the significance, timeliness and services offered by healthcare facilities.

Place of delivery was found to be a significant predictor of the survival time to first ANC visit. Women whose last birth was in Home had a 35% longer survival time to start a first ANC visit compared to those whose last birth was in Health facility. This result is supported by the finding reported from Western Ethiopia in which women whose previous childbirth was institutional delivery were five times more likely to initiate ANC early when compared with women who had a home delivery.(43) A study from Mandera County in Kenya reported that women who utilized skilled delivery service were more likely to have used ANC services more than those who had not utilized the service.(38) A possible explanation might be that mothers who gave birth at health institutions might receive advice and relevant information regarding the importance of early antenatal booking for themselves and their fetuses, which might positively influence women's attitudes towards early ANC visits.

This study showed that women whose last birth was caesarean section had a 25% shorter time to start first ANC than those who gave their last birth vaginally. This finding is supported with previous similar studies.(36,38,44) A study done in Uganda showed that women who gave birth by caesarean section were more likely to initiate the first ANC visit in the first trimester of

pregnancy.(44) According to a study from Tanzania, women with a history of previous or current pregnancy-related complications were more likely to book earlier than others.(36) In Kenya, women who had complications during last pregnancy were two times more likely to utilize ANC than those who had no complication.(38) This might be due to the fact that women who had complications in the previous pregnancy might have worries about them-selves and their fetus's health which compels them to better use antenatal care services.

Regarding geographical region of the country, women from SNNPR had a 46% prolonged time to start first ANC compared to women from Addis Ababa. This might be related to the difference in availability of health facilities. The population in the SNNPR is more dispersed making the accessibility of health facilities difficult, and women from those areas might be less informed about the benefits of antenatal care. Additionally, women from Harari were found to have a shorter time to commence ANC.

Study limitations and strengths

This study used secondary data that were collected cross-sectionally through self-reported interviews, which are prone to recall errors and social desirability bias. In addition, some factors that are probably crucial in determining the timing of the first ANC visit were not available for consideration in the existing EMDHS data, such as the standard of ANC provided and women's perceptions of the ANC. Despite these drawbacks, the current study used a large sample from nationally representative survey data in Ethiopia. The study's findings were representative of all regions. The study also attempted to analyze community-level variables related to the survival time to first ANC visit. Another advantage of the study is its sophisticated statistical design, which allows for greater reliability of the results and allows for the control of confounding factors.

Conclusion

The study indicated that women in the study area sought their initial antenatal care at a health facility far later than the WHO recommended. The independent predictors, women's education level, media exposure, and prior cesarean delivery made early ANC initiation possible. Increasing parity, being previously in a union, having a home birth, and living in a rural area were the impediments for early ANC initiation.

It's crucial to provide health education with a focus on empowering expectant mothers to timely activate prenatal care, especially for those who give birth at home and for those who reside in remote areas. Healthcare providers should collaborate with community health workers to provide home-based care in order to encourage prompt ANC among hard-to-reach populations, such as rural residents and those giving birth at home.

This study also has the implication that policies aiming to decrease pregnancy-related preventable morbidity and mortality through the use of timely antenatal care must prioritize educating and empowering women.

Abbreviations and Acronyms

AAF: Adjusted Acceleration Factor; AFT: Accelerated Failure Time; ANC: Antenatal Care; CI: Confidence Interval; DHS: Demographic and Health Survey; EMDHS: Ethiopian Mini Demographic and Health Survey; ICC: Intraclass Correlation Coefficient; MAF: Median Acceleration Factor; PCV: Proportional Change in Variance; PNC: Postnatal Care.

Funding

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Availability of data

The data sets recoded and analyzed during this study are available in the Measure DHS program repository to all registered users (https://www.dhsprogram. com/data/dataset_admin)

Declarations

Ethics approval and consent to participate

Ethics review and participant consent were not required for this study because it used secondary data analysis of publicly available survey data from the Measure DHS program. A written letter of permission was secured from the IRB of Demographic and Health Survey (DHS) program data archivists to download and use the data for this study from https://www.dhsprogram.com. This study was performed in line with the principles of the Declaration of Helsinki. The DHS

data were kept confidential, and any identifying information was removed. The data was only used for this particular, authorized research project, and it would not be shared with any researchers.

Competing interests

The authors declare that they have no competing interests.

Acknowledgment

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Author contributions

BTO and HZA conceived the study, participated in its design and coordination, initiated the research, carried out the statistical analysis, interpreted the results, and wrote the final manuscript, critically reviewing it. MA and DGT participated in the study's design, guided the statistical analysis, and critically reviewed the manuscript. HI and TG were involved in principal supervision, participated in the study's design and coordination, edited the manuscript, and critically reviewed the manuscript.BTO has main responsibility for the final content, and makes the decision to publish. The authors have read and approved the final manuscript.

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Table 1 Summary of individual and community level factors of time to ANC initiation among study participants (2924), 2022

Covariates	Categories	Time to ANC initiation		Total N (%)
		Event N (%)	Censored N (%)	
Maternal education	Higher	105(68.6)	48(31.4)	153(5.2)
	Secondary	130(38.8)	205(61.2)	335(11.5)
	Primary	452(39.2)	701(60.8)	1153(39.4)
	No education	404(31.5)	879(68.5)	1283(43.9)
Wealth Index	Rich	647(48)	701(52)	1348(46.1)
	Middle	182(31)	407(69)	589(20.1)
	Poor	264(26.7)	723(73.3)	987(33.8)
Household size (members)	1-5	692(43.3)	907(56.7)	1599(54.7)
	6 or more	401(30.3)	924(69.7)	1325(45.3)
Maternal age	<20 years	48(31.4)	105(68.6)	153(5.2)
	20-34 years	846(39.2)	1310(60.8)	2156(73.8)
	≥35 years	199(32.4)	416(67.6)	615(21)
Household head	Female	156(40.4)	230(59.6)	386(13.2)
	Male	937(36.9)	1601(63.1)	2538(86.8)
Place of delivery	Facility	801(42.4)	1088(57.6)	1889(64.6)
	Home	292(28.2)	743(71.8)	1035(35.4)
PNC	No	881(36.5)	1532(63.5)	2413(82.5)
	Yes	212(41.5)	299(58.5)	511(17.5)
Last birth C/S	No	804(34.9)	1502(65.1)	2306(92.2)
	Yes	114(58.5)	81(41.5)	195(7.8)
Birth interval (2220)	≥36 months	478(37.6)	792(62.4)	1270(57.2)
	<36 months	305(32.1)	645(67.9)	950(42.8)
Ever had a child loss	No	939(39.7)	1429(60.3)	2368(81)
	Yes	154(27.7)	402(72.3)	556(9)
Parity	Primi-para	299(43.4)	390(56.6)	689(23.6)
	Multipara	559(40.8)	811(59.2)	1370(46.8)
	Grand Multipara	235(27.2)	630(72.8)	865(29.6)
Residence	Urban	445(51)	427(49)	872(29.8)
	Rural	647(31.5)	1405(68.5)	2052(70.2)

Community ANC utilization	High	718(43.3)	937(56.6)	1655(56.6)
	Low	375(29.6)	894(70.4)	1269(43.4)
Community women education	High	696(39.7)	1056(60.3)	1752(59.9)
	Low	397(33.9)	775(66.1)	1172(40.1)
Community level poverty	Low	740(46.9)	837(53.1)	1577(53.9)
	High	353(26.2)	994(73.8)	1347(46.1)

Note: ANC = antenatal care; PNC = postnatal care; C/S = cesarean section

Table 2 Comparison of survival time of individual and community level factors of time to ANC initiation among study participants (2924), 2022

Covariates	Categories	Time to ANC initiation		Log-rank test	P-value
		Event observed	Event expected		
Mothers education	No education	404	488	114.88	0.0001
	Primary	452	431		
	Secondary	131	126		
	Higher	105	47		
Household size	<6 members	692	585	54.22	0.0001
	≥6 members	400	507		
Ever had a child loss	No	938	876	28.21	0.0001
	Yes	154	216		
Women age	<20 years	49	57	11.48	0.0032
	20-34 years	845	802		
	≥35 years	198	233		
Birth interval	≥36 months	477	442	8.49	0.0036
	<36 months	305	340		
PNC	No	881	909	6.82	0.0090
	Yes	211	183		
Marital status	Currently in union	1030	1029	4.53	0.1039
	Formerly in union	54	59		
	Never in union	8	4		
Household head	Female	156	140	2.68	0.1018
	Male	936	952		
Community level poverty	Low	739	569	136.88	0.0001
	High	353	523		
Residence	Urban	445	310	105.30	0.0001
	Rural	647	782		
Community ANC utilization	High	717	606	58.21	0.0001
	Low	375	486		
Community women education	High	695	645	12.27	0.0005
	Low	397	447		

Note: ANC = antenatal care; PNC = postnatal care

Table 3 Measures of variation and model fit statistics for time to first ANC visit among women in Ethiopia, 2023

	Null model	Model II	Model III	Model IV
Random effect result				
Variance	0.7686926	0.519486	0.4981052	0.4178334
ICC (%)	18.9	13.6	13.1	11.3
PCV (%)	Reference	32.4	4.12	16.1
MAF	2.31	1.99	1.96	1.85
Model fit statistics				
-Log likelihood	-2343.361	-2086.979	-2281.065	-2010.789
AIC	4692.722	4203.958	4594.130	4075.578
DIC	4686.722	4173.958	4562.130	4021.578

Table 4 Mixed-effects Weibull AFT survival regression of time to first ANC visit among women in Ethiopia, 2023

Variables	Categories	Null Model	Model II	Model III	Model IV
Place of last birth	Facility		1		1
	Home		1.11(0.98, 1.25)		1.35(1.13, 1.61)**
Parity	Primipara		1		1
	Multipara		1.09(0.96, 1.25)		1.07(0.89, 1.28)
	Grand multipara		1.19(1.03, 1.40)*		1.31(1.04, 1.63)*
Media Access	No		1		1
	Yes		0.83(0.73, 0.94)**		0.90(0.76, 1.06)
Last birth	Vaginal		1		1
	C/S		0.86(0.75, 0.98)*		0.75(0.61, 0.93)**
Educational level	No formal education		1		1
	Primary		0.97(0.87, 1.09)		0.87(0.73, 1.03)
	Secondary		1.16(1.01, 1.34)*		0.99(0.75, 1.33)
	Higher		0.84(0.70, 0.99)*		0.69(0.50, 0.95)*
Marital status	Currently in union		1		1
	Formerly in union		1.12(0.88, 1.44)		1.47(1.07, 2.00)*
	Never in union		0.64(0.37, 1.09)		1.12(0.37, 3.40)
PNC	No		1		1
	Yes		0.87(0.75, 1.00)		0.83(0.67, 1.02)
Community ANC	Low			1	1
	High			0.95(0.85, 1.07)	0.90(0.77, 1.05)
Community Education	Low			1	1
	High			0.95(0.85, 1.06)	1.15(0.99, 1.34)
Residency	Urban			1	1
	Rural			1.15(1.01, 1.32)*	1.25(1.03, 1.52)*
Region	Addis Ababa			1	1

	Tigray			1.20(0.96, 1.48)	1.04(0.80, 1.35)
	Afar			1.07(0.85, 1.34)	0.93(0.69, 1.24)
	Amhara			1.03(0.81, 1.31)	0.95(0.72, 1.26)
	Oromia			1.37(1.12, 1.68)**	1.08(0.81, 1.43)
	Somalia			1.03(0.68, 1.57)	1.17(0.81, 1.70)
	Benishangul			1.21(0.97, 1.52)	1.19(0.89, 1.60)
	SNNPR			1.50(1.23, 1.84)***	1.46(1.02, 2.10)*
	Gambella			1.39(1.11, 1.73)**	1.23(0.92, 1.65)
	Harari			0.97(0.79, 1.21)	0.80(0.65, 0.99)*
	Dire Dawa			0.93(0.76, 1.15)	0.82(0.65, 1.05)

Note: P-value: * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$, 1 = Reference category

Figure 1 Mixed-effects AFT Weibull regression of time to first ANC visit by place of residence

Supplemental Table 1 Comparison of Mixed-effects AFT model with different baseline distributions

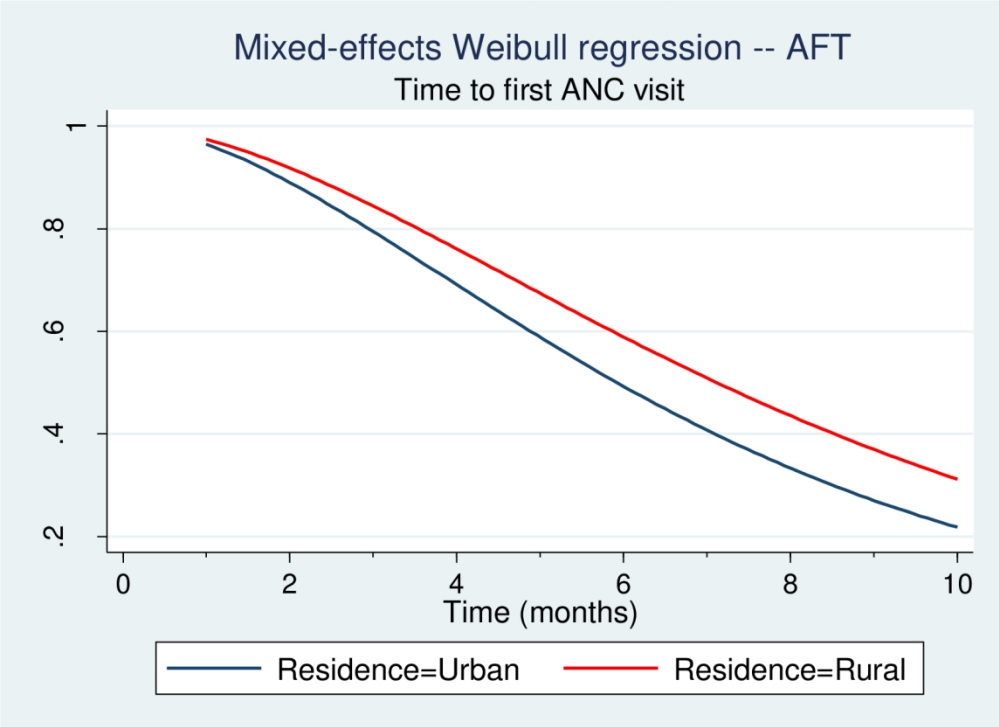

Figure 1 Mixed-effects AFT Weibull regression of time to first ANC visit by place of residence

139x101mm (300 x 300 DPI)

Supplemental Table 1 Comparison of Mixed-effects AFT model with different baseline distributions

Model	Parameters	-Log Likelihood value (Full)	DIC value	AIC value	BIC
Exponential	26	-2990.973	5981.947	6033.947	6185.538
Weibull	27	-2010.789	4021.578	4075.578	4232.999
Log-normal	27	-2771.332	5542.664	5596.664	5754.086
Log-logistic	27	-2797.825	5595.650	5649.650	5807.071
Gamma	27	-2817.554	5635.108	5689.108	5846.530

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3-5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5-6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	6
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*5-8*
Bias	9	Describe any efforts to address potential sources of bias	
Study size	10	Explain how the study size was arrived at	5-6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8-10
		(*b*) Describe any methods used to examine subgroups and interactions	8
		(*c*) Explain how missing data were addressed	
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	

Continued on next page

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	10-11
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10-11
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	*10*
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	13
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	18
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14-17
Generalisability	21	Discuss the generalisability (external validity) of the study results	18
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	19

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Time to initiation of antenatal care and its predictors among pregnant women in Ethiopia: Multilevel Mixed-effects Acceleration Failure Time model

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Time to initiation of antenatal care and its predictors among pregnant women in Ethiopia: Multilevel Mixed-effects Acceleration Failure Time model

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Abstract

Objective: To assess the time-to-initiation of antenatal care and its predictors among pregnant women in Ethiopia.

Design: Retrospective follow-up study using secondary data from the 2019 Ethiopian mini demographic and health survey.

Setting and participants: 2933 women aged 15 to 49 who had ANC visit during their current or most recent pregnancy within the five years prior to the survey were included in this study. Women who attended prenatal appointments but whose gestational age was unknown at the first prenatal visit were excluded from the study.

Outcome measures: Participants were interviewed to respond the gestational age in months at which they made the first antenatal care visit. Multivariable Mixed-effects survival regression was fitted to identify factors associated with the time-to-initiation of ANC.

Results: In this study, the estimated mean survival time of pregnant women to initiate the first ANC visit in Ethiopia was found to be 6.8 months (95% CI: 6.68, 6.95). Women whose last birth was a caesarean section (AAF = 0.75; 95% CI: 0.61, 0.93), and women with higher education (AAF = 0.69; 95% CI: 0.50, 0.95) had a shorter time to initiate ANC early in the first trimester of pregnancy. However, being grand multiparous (AAF = 1.31; 95% CI: 1.05, 1.63), being previously in a union (AAF = 1.47; 95% CI: 1.07, 2.00), having a home birth (AFT = 1.35; 95% CI: 1.13, 1.61), and living in a rural area (AAF = 1.25; 95% CI: 1.03, 1.52) were the impediments for early ANC initiation.

Conclusion: Women in this study area sought their initial antenatal care far later than the WHO recommended. Therefore, healthcare providers should collaborate with community health workers to provide home-based care in order to encourage prompt ANC among hard-to-reach populations, such as rural residents and those giving birth at home.

Strength and limitations of this study

- This study used a large, nationally representative sample from Ethiopian survey data.
- This study evaluated community- and individual-level factors related to the survival time to initiation of ANC visit using a robust model.
- Many factors that could affect the timing of the first ANC visit were not taken into account in this study because they were not present in the original data.
- Social desirability bias is likely to arise because the data were collected through self-reported interviews with participants.

Introduction

A healthy pregnancy for both mother and child, a smooth transition to a happy labor and delivery experience, and successful parenthood are all aspects of the positive pregnancy experience that women want and need.(1) However, the morbidity and mortality rates associated with pregnancy that are preventable are still too high at the outset of the Sustainable Development Goals (SDG) period. In order to improve the pregnancy's outcome, antenatal care (ANC) is a crucial time for health promotion, screening, and disease prevention.(2) For multidisciplinary care providers, the early antenatal care visit is the best opportunity to intervene with health promotion activities and establish a baseline knowledge of the pregnant woman's pre-existing medical conditions.(3)

Early detection of modifiable risk factors and pre-existing conditions was made possible by timely prenatal care initiation, which is defined as the first antenatal contact made during the first trimester of pregnancy.(4) The 2016 World Health Organization (WHO) recommendation also suggests an early beginning of ANC within the first 12 weeks of gestation.(2) Women with early ANC initiation are more likely to have a sufficient number of antenatal care contacts.(5) A study from low and middle-income countries has shown that receiving early ANC is associated with a higher likelihood of having an eight-plus ANC visit.(6) According to a Pakistani study, women who had their first ANC checkup within three months of being pregnant were more likely to obtain WHO-recommended services during their pregnancy, indicating that the timing of the checkup is a strong predictor of the content of services.(7)

There has been a significant improvement in the estimated global coverage of early prenatal care visits, going from 40.9% in 1990 to 84.8% in 2013, or a 43.3% increase.(4) The estimated coverage

of early prenatal care visits in low-income countries (LMICs) in 2013 was 24 percent, compared to 81 percent in high-income countries.(4) Data from these nations' Demographic Health Surveys (DHS) from 2012 to 2018 show that this percentage has climbed to 44.3%.(5) Yet, this shows that the rate of early initiation of ANC in the LMICs is very far from the optimal level.

A woman dies every two minutes due to pregnancy or childbirth, according to United Nations (UN) estimates.(8) The poorest nations and those experiencing conflict continue to have the highest rates of maternal fatalities. With 3.6% of all maternal deaths worldwide in 2020, Ethiopia had the fourth-highest estimated number of maternal deaths, behind the Democratic Republic of the Congo, Nigeria, and India.(8) Timely ANC initiation is essential to lowering maternal morbidity and mortality in countries with high rates of maternal morbidity and mortality.(9)

The magnitude of timely initiation of ANC visits in Sub-Saharan Africa was 38.0%, ranging from 14.5% in Mozambique to 68.6% in Liberia.(10) In Ethiopia, being one of the SSA countries, the problem is even worse. The median time to antenatal care initiation in the country was found to be 5 months.(11) The result from the 2016 Ethiopian Demographic Health Survey (EDHS) revealed only 20% of pregnant women in Ethiopia start their ANC during the first trimester of their pregnancy.(12) Other studies in the country reported varying magnitudes of early initiation of ANC; the proportion was found to be 46.8% in Bahirdar,(13) 21.71% in southern Ethiopia,(14) 40.6% in Debre Markos,(15) 39.5% in Tselemt district of Tigray Region,(16) 27.5% in Axum,(17) 28.8% in Ilu-Ababor,(18) and 34% in Bench-Sheko zone.(19)

Predictors of timing of first antenatal care follow-up from different literatures were residence,(10,12,20) household wealth,(10,21) educational status of the women,(10,11,17) media exposure,(10,11,20) occupation of the women,(22–24) parity,(11,25,26) husband education,(20,21) husband occupation,(20) distance from health facility,(10,26) and maternal age.(10,21,27)

Despite various studies on identifying risk factors for time to first ANC follow-up conducted in Ethiopia, only a few studies were found to be representative at the national level. Furthermore, almost all of the studies failed to consider community-level factors for the time to the initiation of ANC in Ethiopia. Updated and nationally representative information is very crucial for policymakers and other concerned bodies to improve the level of early antenatal care initiation.

Respecting women's rights and providing them with early prenatal care is the first step in a lifetime of care that will improve both the mother and child's health.(3) Therefore, this study undertook a retrospective analysis based on the 2019 Ethiopian Mini Demographic and Health survey (EMDHS) data set, to identify time-to-initiation of ANC and its predictors in Ethiopia.

Methods

Study design and area

This study undertook a retrospective analysis based on the 2019 Ethiopian Mini Demographic and Health Survey (EMDHS) data set. Ethiopia is located in the Horn of Africa and shares a border with Eritrea, Djibouti, Somalia, Sudan, South Sudan, and Kenya. It has a population number of over 110 million people putting it second in Africa.(28) The 2021 World Bank report indicated that, Ethiopia had a gross national income per capita of US$ 940.(29)

Data source and sampling procedure

Data from the 2019 Ethiopian Mini Demographic and Health Survey (EMDHS) were used in this study. The data were supplied once the Measure DHS website (http://www.measuredhs.com) was contacted online and the goal of the study was explained. (30) The variables included in this study were found in the under-five children's file (KR) and individual women's files (EMDHS 2019). Interviews with permanent residents and guests who had been in the dwellings the day before the survey were done in person with the 2019 EMDHS sample, which had been stratified and selected in two steps. (30) A composite of all census enumeration areas (EAs) made for the 2019 Ethiopia Population and Housing Census (PHC), which will be conducted by the Central Statistical Agency (CSA), is the 2019 EMDHS sample frame. The whole list of 149,093 EAs prepared for the 2019 PHC is included in the census frame. A geographic area of 131 households on average is called an EA. The location of the EA, the kind of dwelling (rural or urban), and the approximate number of residential households are all included in the sampling frame.(30)

Study population

All women aged 15 to 49 who had ANC during their current or most recent pregnancy within the five years prior to the survey were included in this study. Women who attended prenatal appointments but whose gestational age was unknown at the first prenatal visit were excluded from

the study. A total of 2933 women aged 15 to 49 who had ANC visits during their current or most recent pregnancy were therefore analyzed in this study.

Study variables

Outcome of interest

The time in months that pregnant women take to receive ANC for the first time is the dependent variable. The event of interest considered as success (event = 1) if women had antenatal care in the first trimester of pregnancy and otherwise censored (censored = 0).

Independent variable

Individual level factors Women's education level, marital status, birth interval, number of prenatal care visits, age, and exposure to the media were all individual-level factors.

Community-level factors were home, area, educational attainment in the community, ANC coverage in the community, and poverty of the community. The only information the EMDHS gathered about the clusters' characteristics was their area and place of residence. Consequently, by combining our interest in a cluster with the individual traits, more shared community-level data were produced. The percentage of a given variable's subcategory that we were interested in within a specific cluster was used to calculate the aggregates. Due to the non-normal distribution of the total generated variable value. The national median values were used to group it into categories.

The aggregates were created using the percentage of a variable's subcategory in a specific cluster. Due to the non-normal distribution of the aggregate value for all newly produced variables, it was divided into two groups (low and high proportions) according to their median values. The percentage of women in the cluster with secondary or higher education is used to gauge the level of education among women in the community. The percentage of women in the cluster's bottom two household wealth quantiles—the poorer and the poorest—was used to define poverty at the community level. The community's use of ANC was determined by looking at the proportion of women in a cluster who use it. Residence location and region were used in the EMDHS data collection according to their classifications.

Operational definition

Exposure to mass media: defined as the frequency of watching television and listening to the radio, excluding exposure to magazines and newspapers. Women who were exposed to radio or

television at least once a week were classified as exposed, whereas those who were not exposed at all were classified as not exposed.

Community women's education: The percentage of mothers in the cluster who completed their elementary, secondary, or tertiary education. The aggregate of primary, secondary, or post-secondary education that each mother has completed can be used to determine the general level of education among the women in the cluster. This variable was split into two groups based on the national median value: a low percentage cluster and a high proportion cluster.

Antenatal care utilization: was defined as mothers who had visited a prenatal care at least four times. (2)

Community antenatal coverage: the percentage of women within the clusters who received four or more prenatal visits (ANC) from a qualified practitioner before their most recent delivery.

Community poverty status: It is defined as the percentage the clusters' poor or poorest mothers.

Data Quality Control and Assurance

The data sets for the original work were collected by face-to-face interviewing women using structured questionnaires that met the eligibility criteria. The woman's questionnaire, the household questionnaire, and the Health Facility Questionnaire were employed to gather essential information. After the questionnaires were finalized in English, they were translated into Amarigna, Tigrigna, and Afaan Oromo. To maintain consistency, the collected data was also back-translated into English. The quality of the dataset has maintained by testing its completeness. Additionally, interviewers were trained to preserve the original data set's quality, and they recorded interviewee responses on tablet computers.

For this study, the data were weighted using sampling weight before any statistical analysis to restore the representativeness of the data and to get a reliable estimate and standard error. The weighted results from the analysis were reported in the study. Multicollinearity between independent variables was checked using Variance Inflation Factor (VIF) and the mean VIF was 2.11. The proportional hazards (PH) assumption was tested using Scaled Schoenfeld residuals and found to be unsatisfied, with a global test value of 0.0001. The data was also assessed for an interaction factor.

Data Management and Analysis

STATA version 14 software was used for cleaning, recoding, and analyzing the data. Descriptive statistics were applied using frequencies and percentages. The Kaplan-Meier survival curve was used to estimate the probability of survival. Survival curves were compared by log-rank test. Univariable survival regression was fitted for explanatory variables and those having p-value ≤0.25 level of significance were considered for the multivariable analysis. Then, the study applied a stepwise backward variable selection procedure to obtain the final reduced model. The proportional hazards (PH) assumption was tested using Scaled Schoenfeld residuals and found to be unsatisfied, with a global test value of 0.0001. A multivariable mixed-effects parametric survival regression model of the Weibull distribution was then fitted. Adjusted Acceleration Factor (AAF) or Time ratio with its 95% confidence interval (CI) was applied, and covariates with a P-value <0.05 in the multivariable analysis were considered determinants of the survival time to first ANC visit.

Survival analysis

Survival analysis deals with the analysis of survival data, which is used to measure the time to an event of interest, such as death or failure.(31) The Cox proportional hazard model is one of the most widely used regression model types in survival analysis. The Cox model estimates the hazard ratio, which is always a nonnegative value. The primary attribute of the Cox model is its reliance on the proportional hazards assumption, which states that "coefficients of the hazard function must remain constant across time for a given covariate".(31)

Parametric acceleration failure time model

An acceleration failure time model (AFT) is a parametric model in the statistical field of survival analysis that offers an alternative to the often used PH models. The primary distinction between Cox model and AFT is that the baseline hazard function is supposed to follow a specific distribution in AFT models. Covariate multiplies the hazard by a constant in a PH model, while it accelerates or decelerates a failure status's life cycle (initiation, discontinuation, disease, death or recovery) by a constant in an AFT model.(32)

Accelerated Failure Time (AFT) model is a model used for adjusting survivor functions for the effects of covariates. The AFT parameterization expresses the natural logarithm of the survival time, log t, as a linear function of the covariates. (31)

$$\log(tj) = Xj\beta + Zjuj + vj \quad \ldots\ldots 1$$

for j = 1, . . . , M clusters with cluster j consisting of i = 1, . . . , nj observations. The vector x_{ji} contains the covariates for the fixed effects, with regression coefficients (fixed effect) β. The vector z_{ji} contains the covariates corresponding to the random effects uj. **v***ji* are observation-level errors with density ϕ(·). The distributional form of the error term determines the regression model. Five regression models are implemented in mestreg using the AFT parameterization: exponential, gamma, loglogistic, lognormal, and Weibull. As a result, this study applied a random-effects Weibull model with normally distributed random effects. This model can be described as a shared frailty model with lognormal frailty.

Mixed-effects parametric survival analysis

The EMDHS employed a multistage cluster sampling technique in which data were hierarchical (pregnant women were nested within families, and households inside clusters).

Considering the hierarchical nature of EMDHS data, pregnant women who lived within the same cluster may have had similar characteristics compared to those who reside in other clusters of the Country. Therefore, a two-stage multivariable mixed-effects parametric survival regression analysis was employed to estimate the effects of individual and community level predictors on the survival time to first ANC visit. Mixed-effects survival models contain both fixed effects and random effects.

Four models were fitted to identify community and individual level factors associated with survival time to first ANC visit. The first model (Model 1, or the empty model) had no explanatory variables. The second model (Model 2) examined the individual-level effect by focusing solely on individual-level factors. The third model (Model 3) evaluated solely the community-level variables to examine the effect of community-level characteristics on the survival time to the first ANC visit, independent of other factors.

The fixed effect sizes of individual and community-level determinants of the survival time to first ANC visit were expressed as AAFs with 95% CI. The P-value <0.05 has been considered as statistically significant. Additionally, the measure of variance (random effects) was reported in terms of the intraclass correlation coefficient (ICC), median acceleration factor (MAF), and proportional change in variance (PCV). Model fitness was checked using Akaike Information

Criteria (AIC) and Deviance Information Criteria (DIC). The lowest AIC and DIC values declare the best fit model.(31)

Patient and public involvement

Women in their reproductive years who had ANC during their current or most recent pregnancy within the five years prior to the survey took part in this study and contributed vital data. However, they never participated in conducting the study, designing the protocol or instruments used to gather the study's data, reporting the findings, or distributing them.

Result

Descriptive statistics

Weighted samples of 2924 women were followed for a minimum of 1 and a maximum of 10 months with an average follow up time of 4 months. In this study, timely initiation of ANC visit in Ethiopia was found to be 42.7% (95% CI: 41.0 – 44.6). The estimated mean (restricted) survival time of pregnant women to initiate the first ANC visit was 6.8 months (95% CI: 6.68, 6.95). The overall incidence rate was approximately 11 per 100 person month of observation. Majority 2755 (94.2%) of women were currently married or inunion, and of these 1030 (37.4%) had initiated ANC visit early in the first trimester of pregnancy. Regarding women education, 1283 (43.9%) women had no education, and among these 404(31.5%) initiated their ANC visit timely. Access to media was reported by 1259(43.1%) of whom 582(46.2%) had started ANC visit within 12 weeks of pregnancy. More than half 114(58.5%) of women who gave birth by C/S started their first ANC visit within the first trimester (Table 1 Summary of individual and community level factors of time to ANC initiation among study participants (2924), 2022).

Most 2052(70.2%) of the women were rural residents, and among these only 647(31.5%) women initiated ANC visit within the recommended time. The proportion of women starting first ANC visit within the first trimester was higher in Harari (66.7%), Dire Dawa (66.7%) and Addis Ababa (65%), whereas lower in the SNNPR (28.8%), Oromia (33.2%) and Somali (33.3%) regional states. More than half 1577(53.9) of the women were from a community with a low poor proportion of whom 740(46.9%) commenced their first ANC visit in the first three months of pregnancy. Moreover, 353(26.2%) women from a community with a high poor proportion commenced their

first ANC visit timely (Table 1 Summary of individual and community level factors of time to ANC initiation among study participants (2924), 2022).

Comparison of the different covariate in terms of survival time to first ANC visit

Kaplan Meier graphs are generated to observe the difference in the survival time to first ANC visit of women for different categorical variables. The log-rank test was carried out to validate the difference between the groups of each categorical variable. The log-rank test result (Table 2) shows that there is statistically significant difference in the survival experience of groups among women education level ($p < 0.0001$), wealth index ($p < 0.0001$), delivery place ($p < 0.0001$), parity ($p < 0.0001$), media access ($p < 0.0001$), region ($p < 0.0001$), women age ($p < 0.001$) and Marital status ($p < 0.2$) (Table 2 Comparison of survival time of individual and community level factors of time to ANC initiation among study participants (2924), 2022).

Random effects and model comparison

As the multilevel mixed-effects Weibull survival regression analysis results described in Table 3, Model I revealed statistically significant variation in the survival time to first ANC visit of women across communities. Nearly One fifth of the variation in the survival time is attributed to community-level factors (ICC = 18.9%). After adjusting the model for individual-level factors (Model II), about 32.4% of the variation in the accelerations of survival time was attributed to the individual level factors (PCV = 32.4%), and 13.6% of the variance in the survival time was attributed to community-level factors (ICC = 13.6%). Model III, which was adjusted for community-level factors, revealed that the community level factors explained 4.12% of the variability in the accelerations of survival time to first ANC visit of women (PCV = 4.12%), and 13.1% of the variation among the clusters was attributed to community-level factors (ICC = 13.1%) (Table 3 Measures of variation and model fit statistics for time to first ANC visit among women in Ethiopia, 2023).

The final best-fit model (model IV) was adjusted for both individual and community-level factors simultaneously. In this final model (model IV), as indicated by the PCV, 16.1% of the variation in the survival time across communities was explained by both individual and community-level factors. Including both individual- and community-level factors reduced the unexplained heterogeneity in the time to first ANC visit between communities from MAF of 2.31 in the null model to the MAF of 1.85 in the final model, which equals 0.46. This showed that the survival

time to first ANC visit reduced by 54% when a woman moved from high risk to low-risk neighborhoods (Table 3 Measures of variation and model fit statistics for time to first ANC visit among women in Ethiopia, 2023).

Based on the AIC and DIC, Multilevel mixed-effects Weibull survival model (Model IV) was found the best model to fit the data with a minimum AIC and DIC values of 4075.578 and 4021.578, respectively ""Supplemental Table 1"".

The survival plot in **Error! Reference source not found.** shows that the survivor function for rural women is above the survivor function for urban women. This implies that rural women have a greater probability of not initiating an ANC visit at earlier gestational age (**Error! Reference source not found.**).

Interpretation of the multilevel Weibull model results

The results of multivariable multilevel parametric Weibull survival analysis of predictors of the survival time to first ANC visit is provided in Table 4 (Table 4 Mixed-effects Weibull AFT survival regression of time to first ANC visit among women in Ethiopia, 2023). The place of delivery was found to have a significant effect on the time to ANC initiation. Home delivered mothers have a 35% (AAF = 1.35; 95% CI: 1.13, 1.61) longer survival time to start a first ANC visit. In other words, home-delivered mothers were less likely to initiate their first ANC visit within the first trimester of pregnancy compared to women who gave birth at a health facility. Similarly, Grand multiparous women have a 31% longer time to start ANC early in the first trimester than primipara women. The acceleration factor for Grand multiparous women was 1.31 (95% CI: 1.05, 1.63).

Women with higher education had a 31% shorter time to start their first ANC visit than those who were not educated (AAF = 0.69; 95% CI: 0.50, 0.95). This indicates that women with higher education are more likely to initiate their first ANC visit in the first 12 weeks of pregnancy than women with no formal education. Similarly, women whose last birth was caesarean section had a 25% shorter time to initiate ANC early in the first trimester as compared to those who delivered vaginally (AAF = 0.75; 95% CI: 0.61, 0.93) (Table 4 Mixed-effects Weibull AFT survival regression of time to first ANC visit among women in Ethiopia, 2023).

Formerly married or in union women took 1.47 times longer (AAF = 1.47; 95% CI: 1.07, 2.00) to schedule their first antenatal care visit early in pregnancy. It can be stated that women who had previously been in unions were less likely to begin their ANC visit early in the first three months of pregnancy than women who were currently in unions (Table 4 Mixed-effects Weibull AFT survival regression of time to first ANC visit among women in Ethiopia, 2023).

The survival time until the first ANC visit was found to be significantly influenced by one's place of residence. Compared to women from urban residences, those from rural ones took 1.25 times longer to begin their first ANC visit early in pregnancy (AAF = 1.25; 95% CI: 1.03, 1.52). In other words, compared to women who lived in urban areas, women who live in rural areas had a lower likelihood of scheduling their first ANC visit during the first 12 weeks of pregnancy. Administrative region was also a significant predictor of time to first ANC visit (Table 4 Mixed-effects Weibull AFT survival regression of time to first ANC visit among women in Ethiopia, 2023).

Discussion

In this study, Ethiopian pregnant women's time-to-initiation of ANC and its predictors were evaluated. Pregnant women's mean survival time to schedule their first ANC check was thus 6.8 months (95% CI: 6.68, 6.95). Furthermore, the time-to-initiation of ANC was significantly associated with factors such as women's educational attainment, prior cesarean birth, parity, marital status, place of delivery, place of residency, and region of residency.

The mean survival time of pregnant women to initiate ANC visit in this study was significantly higher than a study done in India in which the reported median survival time to first ANC visit was 4 months. (33) The finding of this study is also slightly higher than the study finding from Nigeria in which the median survival time for the first ANC checkup was found to be 6 months.(34) Moreover, this finding is higher when compared to the recent findings of average of 3.4 gestational months before initiation of ANC visit in Ghana.(27) However, late initiation of ANC visit has been previously reported in Ethiopia with a median survival time of 7 months.(35)

Timely initiation of ANC visit within the first three months of pregnancy in Ethiopia was found to be 42.7% (95% CI: 41.0, 44.6). This finding is lower than the study conducted in Pakistan which

indicated that nearly half of women (48%) received ANC within 3 months of pregnancy.(7) This finding is significantly higher than studies done in Tanzania,(36) Benin,(37) Kenya,(38) and Nigeria,(34) but lower compared to a study from Ghana, where first trimester initiation of ANC visit was reported to be as high as 57%.(27) This result is higher than the previous study conducted in Ethiopia that reported timely initiation of ANC visit of 38.6%.(35)

Women who had higher education had a 31% shortened time to start first ANC visit than those with no formal education. This finding is in agreement with findings of previous studies. (11,33,39) A study conducted in India revealed that women with higher education had a 2.8 times shorter time to initiation of ANC in the first trimester of pregnancy compared to women having no formal education.(33) Similarly, in Nepal, women with higher level education were significantly more likely to initiate ANC early compared to women who had no education.(39) A multi-country analysis of DHS in SSA found that the odd of timely initiation of ANC was higher in mothers who had higher level of education compared to women who had no formal education.(10) A study from Nigeria revealed that women with higher education were more likely to start first ANC visit early compared to uneducated women.(34) A retrospective study from Ethiopia revealed that early initiation of ANC increases as the women's level of education increases compared to women who have no formal education.(11)

The possible explanation could be due to women with a higher level of education might be more likely to be employed, financially independent, and knowledgeable on the necessity of having antenatal care follow-up during pregnancy, as a result, they might be more likely to realize the importance of early booking their first ANC visit timely.(40) Additionally, uneducated women might have limited understanding of ANC services and their importance to their unborn fetus wellbeing and ensure safe delivery.(11) It is because education will change the knowledge when to start ANC awareness of the mothers to start and follow the health services appropriately.(18)

This study indicated that women who were formerly in union commenced ANC visit later than mothers who were currently in union at 5% level of significance. The findings of this study indicate that having the father of the child present in the woman's life during pregnancy shortens the time to first ANC attendance and highlight a need to involve male partners in reproductive health issues including maternal health care and family planning. This evidence is in line with the studies done

in South Africa(24) and Rwanda(26) in which currently married women were more likely to initiate ANC in the first trimester of pregnancy.

This might be due to the fear of social rumors, and hence, lack of confidence in seeking care for unborn child whose father is not formal or in doubt. Another possible explanation can be the work load hanged on her shoulder only to improve the life of her unborn child and herself too. Furthermore, they might not know whether they are pregnant timely, and even if they knew it early, they may not be interested with the pregnancy, they may be careless for the conception and fail to book early. Women with an unwanted (24) and mistimed pregnancies (41) have been show to receive late ANC.

Grand multiparous women had a 31% longer time to start ANC early in the first trimester than primipara women. This evidence is supported by prior studies.(11,33,41,42) A study finding from India has shown that women with birth order of 4 and above had a 16% prolonged time to initiation of ANC compared to Primipara women.(33) In Malawi, women with more than five births were 12% less likely to access ANC services in their first trimester of pregnancy.(42) In Nigeria, women with one birth were more likely to initiate ANC in the first trimester compared to women with five and above births.(21) In Kenya, women with four and above births were 1.75 times more likely to start their first antenatal care late in pregnancy during the second and third trimesters of pregnancy compared to the Primipara women.(41)

A survival study from Ethiopia found that women with four and above births had a 20% hazard of delayed initiation of ANC follow up as compared to one parity.(11) Another population study from Ethiopia showed that multi-parous women had higher odds of delayed initiation of ANC visit when compared to the primi-parous women.(23) This might be attributable to high parity women's increased confidence from previous pregnancy and childbirth experience. Additionally, high parity women might have poor prior experience with the health system, and constraints of time and resources to access ANC services early.(38)

This study also showed that women from a rural residency had a prolonged time to start their first ANC visit relative to those who were from an urban residency. In India, urban residents had a 49% probability of initiating ANC early in the first trimester of pregnancy compared to rural counterparts.(33) In SSA, women residing in the rural area were less likely to initiate ANC timely

within 12 weeks of gestation.(10) In Nigeria, women in urban areas were more likely to make the first ANC visit early in the first trimester of pregnancy.(34) A study from Kenya showed that the odds of timely initiation of ANC in the first 3 months of pregnancy was higher in women living in urban areas compared to the rural counterparts.(41)

A study in Ethiopia using the 2016 EDHS data set indicated that rural women have prolonged time-to start first ANC visit than urban women.(20) In Ethiopia, women from rural residency were 18% less likely to attained ANC early in pregnancy than urban counter parts.(11) Another similar study in Ethiopia showed that rural women were 59% less likely to start their first ANC visit within the first trimester than urban counterparts.(12) This might be because urban women have easier access to transportation and social media, which help them easily, obtain information about the significance, timeliness and services offered by healthcare facilities.

Place of delivery was found to be a significant predictor of the survival time to first ANC visit. Women whose last birth was in Home had a 35% longer survival time to start a first ANC visit compared to those whose last birth was in Health facility. This result is supported by the finding reported from Western Ethiopia in which women whose previous childbirth was institutional delivery were five times more likely to initiate ANC early when compared with women who had a home delivery.(43) A study from Mandera County in Kenya reported that women who utilized skilled delivery service were more likely to have used ANC services more than those who had not utilized the service.(38) A possible explanation might be that mothers who gave birth at health institutions might receive advice and relevant information regarding the importance of early antenatal booking for themselves and their fetuses, which might positively influence women's attitudes towards early ANC visits.

This study showed that women whose last birth was caesarean section had a 25% shorter time to start first ANC than those who gave their last birth vaginally. This finding is supported with previous similar studies.(36,38,44) A study done in Uganda showed that women who gave birth by caesarean section were more likely to initiate the first ANC visit in the first trimester of pregnancy.(44) According to a study from Tanzania, women with a history of previous or current pregnancy-related complications were more likely to book earlier than others.(36) In Kenya, women who had complications during last pregnancy were two times more likely to utilize ANC than those who had no complication.(38) This might be due to the fact that women who had

complications in the previous pregnancy might have worries about them-selves and their fetus's health which compels them to better use antenatal care services.

In relation to the country's administrative region, women from SNNPR had a 46% longer time to start the first ANC compared to women from Addis Ababa. One possible explanation for this could be the variations in the accessibility of medical facilities. The population in the SNNPR is more dispersed, making the accessibility of health facilities difficult, and women from those areas might be less informed about the benefits of antenatal care. Additionally, women from Harari were found to have a shorter time to commence ANC.

Study limitations and strengths

This study used secondary data that were collected cross-sectionally through self-reported interviews, which are prone to recall errors and social desirability bias. Furthermore, some factors that are probably crucial in determining the timing of the first ANC visit, such as the standard of ANC provided and women's perceptions of the ANC, were not available for consideration in the existing EMDHS data.

Despite these drawbacks, the current study used a large sample from nationally representative survey data in Ethiopia. The results of the study were representative of all regions. The study also attempted to analyze community-level variables related to the survival time to initiation of the ANC visits. Another advantage of the study is its sophisticated statistical design, which allows for greater reliability of the results and allows for the control of confounding factors.

Conclusion

The study indicated that women in the study area sought their initial antenatal care at a health facility far later than the WHO recommended. Early ANC initiation in the first trimester of pregnancy was positively associated with independent variables, such as women's educational attainment, media exposure, and history of caesarean delivery. Higher parity, home births, rural settlements, and previously formed but unsuccessful unions had a negative effect on the initiation of ANC services during the first trimester of pregnancy.

Therefore, it's crucial to provide health education with a focus on empowering expectant mothers to timely activate prenatal care, especially for those who give birth at home and for those who

reside in remote areas. Healthcare providers should collaborate with community health workers to provide home-based care in order to encourage prompt ANC among hard-to-reach populations, such as rural residents and those giving birth at home. This study also has the implication that policies aiming to decrease pregnancy-related preventable morbidity and mortality through the use of timely antenatal care must prioritize educating and empowering women.

Abbreviations and Acronyms

AAF: Adjusted Acceleration Factor; AFT: Accelerated Failure Time; ANC: Antenatal Care; CI: Confidence Interval; DHS: Demographic and Health Survey; EMDHS: Ethiopian Mini Demographic and Health Survey; ICC: Intraclass Correlation Coefficient; MAF: Median Acceleration Factor; PCV: Proportional Change in Variance; PNC: Postnatal Care.

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Availability of data

The data sets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

Ethics review and participant consent were not required for this study because it used secondary data analysis of publicly available survey data from the Measure DHS program. A written letter of permission was secured from the IRB of Demographic and Health Survey (DHS) program data archivists to download and use the data for this study from https://www.dhsprogram.com. This study was performed in line with the principles of the Declaration of Helsinki. The DHS data were kept confidential, and any identifying information was removed. The data was only used for this particular, authorized research project, and it would not be shared with any researchers.

Competing interests

The authors declare that they have no competing interests.

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Author contributions

BTO and HZA conceived the study, participated in its design and coordination, initiated the research, carried out the statistical analysis, interpreted the results, and wrote the final manuscript, critically reviewing it. MA and DGT participated in the study's design, guided the statistical analysis, and critically reviewed the manuscript. HI and TG were involved in principal supervision, participated in the study's design and coordination, edited the manuscript, and critically reviewed the manuscript. BTO has main responsibility for the final content, and makes the decision to publish. The authors have read and approved the final manuscript.

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Table 1 Summary of individual and community level factors of time to ANC initiation among study participants (2924), 2022

Variables	Categories	Time to ANC initiation	Total N (%)

		Event N (%)	Censored N (%)	
Maternal education	Higher	105(68.6)	48(31.4)	153(5.2)
	Secondary	130(38.8)	205(61.2)	335(11.5)
	Primary	452(39.2)	701(60.8)	1153(39.4)
	No education	404(31.5)	879(68.5)	1283(43.9)
Wealth Index	Rich	647(48)	701(52)	1348(46.1)
	Middle	182(31)	407(69)	589(20.1)
	Poor	264(26.7)	723(73.3)	987(33.8)
Household size (members)	1-5	692(43.3)	907(56.7)	1599(54.7)
	6 or more	401(30.3)	924(69.7)	1325(45.3)
Maternal age	<20 years	48(31.4)	105(68.6)	153(5.2)
	20-34 years	846(39.2)	1310(60.8)	2156(73.8)
	≥35 years	199(32.4)	416(67.6)	615(21)
Household head	Female	156(40.4)	230(59.6)	386(13.2)
	Male	937(36.9)	1601(63.1)	2538(86.8)
Place of delivery	Facility	801(42.4)	1088(57.6)	1889(64.6)
	Home	292(28.2)	743(71.8)	1035(35.4)
PNC	No	881(36.5)	1532(63.5)	2413(82.5)
	Yes	212(41.5)	299(58.5)	511(17.5)
Last birth C/S	No	804(34.9)	1502(65.1)	2306(92.2)
	Yes	114(58.5)	81(41.5)	195(7.8)
Birth interval (2220)	≥36 months	478(37.6)	792(62.4)	1270(57.2)
	<36 months	305(32.1)	645(67.9)	950(42.8)
Ever had a child loss	No	939(39.7)	1429(60.3)	2368(81)
	Yes	154(27.7)	402(72.3)	556(9)
Parity	Primi-para	299(43.4)	390(56.6)	689(23.6)
	Multipara	559(40.8)	811(59.2)	1370(46.8)
	Grand Multipara	235(27.2)	630(72.8)	865(29.6)
Residence	Urban	445(51)	427(49)	872(29.8)
	Rural	647(31.5)	1405(68.5)	2052(70.2)
Community ANC utilization	High	718(43.3)	937(56.6)	1655(56.6)
	Low	375(29.6)	894(70.4)	1269(43.4)
Community women education	High	696(39.7)	1056(60.3)	1752(59.9)
	Low	397(33.9)	775(66.1)	1172(40.1)
Community level poverty	Low	740(46.9)	837(53.1)	1577(53.9)
	High	353(26.2)	994(73.8)	1347(46.1)

Note: ANC = antenatal care; PNC = postnatal care; C/S = cesarean section

Table 2 Comparison of survival time of individual and community level factors of time to ANC initiation among study participants (2924), 2022

Variables	Categories	Time to ANC initiation		Log-rank test	P-value
		Event observed	Event expected		
Mothers education	No education	404	488	114.88	0.0001
	Primary	452	431		
	Secondary	131	126		
	Higher	105	47		
Household size	<6 members	692	585	54.22	0.0001
	≥6 members	400	507		
Ever had a child loss	No	938	876	28.21	0.0001
	Yes	154	216		
Women age	<20 years	49	57	11.48	0.0032
	20-34 years	845	802		
	≥35 years	198	233		
Birth interval	≥36 months	477	442	8.49	0.0036
	<36 months	305	340		
PNC	No	881	909	6.82	0.0090
	Yes	211	183		
Marital status	Currently in union	1030	1029	4.53	0.1039
	Formerly in union	54	59		
	Never in union	8	4		
Household head	Female	156	140	2.68	0.1018
	Male	936	952		
Community level poverty	Low	739	569	136.88	0.0001
	High	353	523		
Residence	Urban	445	310	105.30	0.0001
	Rural	647	782		
Community ANC utilization	High	717	606	58.21	0.0001
	Low	375	486		
Community women education	High	695	645	12.27	0.0005
	Low	397	447		

Note: ANC = antenatal care; PNC = postnatal care

Table 3 Measures of variation and model fit statistics for time to first ANC visit among women in Ethiopia, 2023

	Null model	Model II	Model III	Model IV
Random effect result				
Variance	0.7686926	0.519486	0.4981052	0.4178334
ICC (%)	18.9	13.6	13.1	11.3
PCV (%)	Reference	32.4	4.12	16.1
MAF	2.31	1.99	1.96	1.85
Model fit statistics				
-Log likelihood	-2343.361	-2086.979	-2281.065	-2010.789
AIC	4692.722	4203.958	4594.130	4075.578
DIC	4686.722	4173.958	4562.130	4021.578

Table 4 Mixed-effects Weibull AFT survival regression of time to first ANC visit among women in Ethiopia, 2023

Variables	Categories	Null Model	Model II	Model III	Model IV
Place of last birth	Facility		1		1
	Home		1.11(0.98, 1.25)		1.35(1.13, 1.61)**
Parity	Primipara		1		1
	Multipara		1.09(0.96, 1.25)		1.07(0.89, 1.28)
	Grand multipara		1.19(1.03, 1.40)*		1.31(1.04, 1.63)*
Media Access	No		1		1
	Yes		0.83(0.73, 0.94)**		0.90(0.76, 1.06)
Last birth	Vaginal		1		1
	C/S		0.86(0.75, 0.98)*		0.75(0.61, 0.93)**
Educational level	No formal education		1		1
	Primary		0.97(0.87, 1.09)		0.87(0.73, 1.03)
	Secondary		1.16(1.01, 1.34)*		0.99(0.75, 1.33)
	Higher		0.84(0.70, 0.99)*		0.69(0.50, 0.95)*
Marital status	Currently in union		1		1
	Formerly in union		1.12(0.88, 1.44)		1.47(1.07, 2.00)*
	Never in union		0.64(0.37, 1.09)		1.12(0.37, 3.40)
PNC	No		1		1
	Yes		0.87(0.75, 1.00)		0.83(0.67, 1.02)
Community ANC	Low			1	1
	High			0.95(0.85, 1.07)	0.90(0.77, 1.05)
Community Education	Low			1	1
	High			0.95(0.85, 1.06)	1.15(0.99, 1.34)
Residency	Urban			1	1
	Rural			1.15(1.01, 1.32)*	1.25(1.03, 1.52)*
Region	Addis Ababa			1	1
	Tigray			1.20(0.96, 1.48)	1.04(0.80, 1.35)
	Afar			1.07(0.85, 1.34)	0.93(0.69, 1.24)
	Amhara			1.03(0.81, 1.31)	0.95(0.72, 1.26)
	Oromia			1.37(1.12, 1.68)**	1.08(0.81, 1.43)
	Somalia			1.03(0.68, 1.57)	1.17(0.81, 1.70)
	Benishangul			1.21(0.97, 1.52)	1.19(0.89, 1.60)
	SNNPR			1.50(1.23, 1.84)***	1.46(1.02, 2.10)*
	Gambella			1.39(1.11, 1.73)**	1.23(0.92, 1.65)
	Harari			0.97(0.79, 1.21)	0.80(0.65, 0.99)*
	Dire Dawa			0.93(0.76, 1.15)	0.82(0.65, 1.05)

Note: P-value: * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$, 1 = Reference category

Figure 1 Mixed-effects AFT Weibull regression of time to first ANC visit by place of residence

Supplemental Table 1 Comparison of Mixed-effects AFT model with different baseline distributions

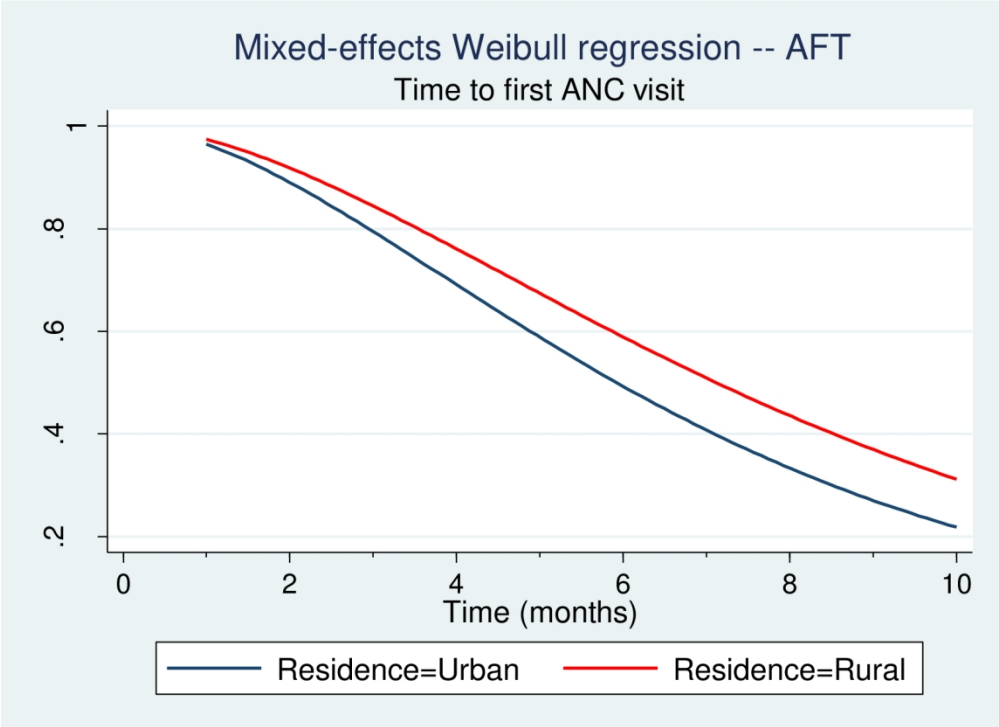

Figure 1 Mixed-effects AFT Weibull regression of time to first ANC visit by place of residence

139x101mm (300 x 300 DPI)

Supplemental Table 1 Comparison of Mixed-effects AFT model with different baseline distributions

Model	Parameters	-Log Likelihood value (Full)	DIC value	AIC value	BIC
Exponential	26	-2990.973	5981.947	6033.947	6185.538
Weibull	27	-2010.789	4021.578	4075.578	4232.999
Log-normal	27	-2771.332	5542.664	5596.664	5754.086
Log-logistic	27	-2797.825	5595.650	5649.650	5807.071
Gamma	27	-2817.554	5635.108	5689.108	5846.530

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3-5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5-6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	6
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	Not Applicable
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*5-8*
Bias	9	Describe any efforts to address potential sources of bias	
Study size	10	Explain how the study size was arrived at	5-6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8-10
		(*b*) Describe any methods used to examine subgroups and interactions	8
		(*c*) Explain how missing data were addressed	
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	Not Applicable
		(*e*) Describe any sensitivity analyses	Not Applicable

Continued on next page

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5-6 and 10
		(b) Give reasons for non-participation at each stage	5-6 and 10
		(c) Consider use of a flow diagram	Not Applicable (eligible and actual study participants were narrated briefly on page 5-6 and 11, respectively)
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10-11
		(b) Indicate number of participants with missing data for each variable of interest	11 (Table 1)
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	10
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	10
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	Not Applicable
		Cross-sectional study—Report numbers of outcome events or summary measures	Not Applicable
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	13
		(*b*) Report category boundaries when continuous variables were categorized	Not Applicable
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not Applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	8 (The data was checked for effect modification or interaction factor)
Discussion			
Key results	18	Summarise key results with reference to study objectives	13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	18
Interpretation	20	Give a cautious overall interpretation of results considering objectives,	14-17

		limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	
Generalisability	21	Discuss the generalisability (external validity) of the study results	18
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	19

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.