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Evaluation of factors related to longitudinal CD4 count and the risk of death among HIV-infected patients using Bayesian joint models

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Abstract

Background In many epidemiological HIV studies, patients are frequently monitored over time to predict their survival by examining their CD4 levels repeatedly. This study aims to evaluate factors related to longitudinal CD4 count and the risk of death among HIV-infected patients using Bayesian joint models.

Methods The information of patients who were infected with HIV in Fars Province, from 2011 to 2016 and followed up until 2022 was used in this study. A joint model of count longitudinal outcome and time to death is used to model information of HIV patients.

Results The majority of patients were male (67.8%) with a median age of 34 years. During the follow-up, 212 patients (28.0%) died. The age-standardized mortality and incidence rates from 2011 to 2016 were 0.496 and 2.49 per 100,000 person-years respectively. The 1-year and 5-year survival rates are 91% (95%CI: 89%, 93%) and 79% (95%CI: 77%, 82%) respectively. There is a significant association in this model between the CD4 cell count and the risk of death. Age, addiction, and men were all significantly linked to CD4 cell count. Age was positively correlated with the risk of death. Men, those with hepatitis B and history of addiction had a higher risk of death.

Conclusion This study uses the power of Bayesian joint models to explore the complex relationship between changes in CD4 counts over time and the risk of death in patients with HIV. Our findings highlight a strong and statistically significant connection between CD4 cell count and mortality risk. By modeling CD4 counts alongside survival data, we offer a deeper understanding of the factors influencing patient outcomes over time, significantly enhancing traditional separate modeling methods. This comprehensive approach leads to more accurate predictions, ultimately aiding in better-informed clinical decisions for HIV care.

Keywords Joint model, CD4 cell count, Longitudinal, Time to death, Association, HIV

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Introduction

Human Immunodeficiency Virus (HIV) remains a significant public health concern globally. According to WHO since the beginning of the epidemic, 85.6 million people have been infected with the Human Immunodeficiency Virus (HIV), and about 40.4 million people have died of HIV. Globally, 39.0 million people were living with HIV at the end of 2022. HIV is also a public health challenge in Iran. According to the latest estimates of the United Nations Program on HIV/AIDS (UNAIDS), a total of 54,000 people were living with HIV, and 3200 people died of HIV at the end of 2020 in IRAN [1]. HIV is an infection that attacks the body's immune system, specifically the white blood cells called CD4 cells. The CD4 count measures how many CD4 cells are present in a person's blood. A normal CD4 count in a healthy adult ranges from 500 to 1,500 cells per cubic millimeter of blood. HIV is considered to have progressed to AIDS (Acquired Immunodeficiency Syndrome) when the CD4 count drops below 200 cells per cubic millimeter of blood. Monitoring CD4 counts is an important part of managing HIV infection. Low CD4 counts indicate a weakened immune system and an increased risk of opportunistic infections [2].

One of the important biomarkers that indicate the weakness of the body's immune system is the number of CD4 cells in a blood sample. Examining and testing the number of CD4 cells and their changes over time is related to the progress of HIV and the death of HIV-infected. It should be noted that the decrease in the number of cells over time can be a sign of deterioration and weakening of the immune system of HIV-infected persons [3, 4]. Observed and follow-up of patients are common in many studies. In these studies, longitudinal measurements were recorded until the time to event of interest and the time origin (baseline) was defined as the time of HIV diagnosis. In many studies, longitudinal and time-to-event responses have been used separately. However, it should be noted that these two responses are related, and modeling them separately can lead to biased results and estimates because such an analysis ignores the association between longitudinal and time-to-event responses. Therefore, the joint modeling of longitudinal and time-to-event responses can lead to unbiased estimates of the parameters describing both processes. In HIV studies, repeated measurements of the CD4 cell count and time of death are always recorded. As mentioned, the CD4 count is the most important clinical measure that indicates disease progression in HIV/AIDS patients earlier than disease or death. Therefore, a joint model was used to consider the dependence between longitudinal and time-to-event responses [5, 6].

Modeling longitudinal and time-to-event data jointly assumes that the longitudinal outcome offers extra insights into the risk of event occurrence, gaining popularity in the medical field over recent decades. Joint models handle the relationship at the individual level and relate the longitudinal and survival components. This approach allows for the simultaneous analysis of repeated measurements of an outcome and time-to-event data in a single model. One of the key advantages of joint modeling is that it can account for the interdependence between the longitudinal and survival outcomes, allowing for a more efficient and accurate estimation of the effects of covariates on both outcomes. This can lead to more precise estimates of the risk factors associated with disease progression and mortality in HIV patients. In this study, we explored factors associated with survival time in HIV-infected individuals using a Bayesian joint model.

Methods

Data collection

In this study, we used the information of patients who were infected with HIV in Fars Province, from June 29, 2011, to March 15, 2016, and they were followed up until May 12, 2022. Demographic and clinical characteristics of patients in the study such as gender, marital status, age, and co-infection with hepatitis B virus (HBV) have been recorded. CD4 cell count from baseline to a maximum of 20 times afterward and time-to-death (time from HIV diagnosis until death due to HIV/AIDS in years) have been recorded. The study protocol was approved by the ethics committee of Shiraz University of Medical Sciences (IR.SUMS.REC.1402.280).

Statistical analysis

The variables were presented as frequency percentages for categorical data and as median values with interquartile ranges for continuous data. A Bayesian joint model was employed to analyze both longitudinal and survival data. This joint model consisted of two components: one component focused on the longitudinal aspect, while the other addressed the survival aspect. To implement the joint model, a generalized linear mixed effects model with a random intercept and slope was utilized for the longitudinal component, and a Cox regression model was applied for the survival component, with the two components linked through unobserved random effects via shared parameters. The outcome variables considered for this study were the longitudinal CD4 count measurement and time to death. Under the Bayesian approach, estimation of the joint model's parameters proceeds using Markov chain Monte Carlo (MCMC) algorithms.

The longitudinal sub-model

We have a set of n independent subjects. Assuming independence between subjects, let Y_{ij} denote the longitudinal response (CD4 cell count) for subject $i = 1, 2, \ldots, n$ at time j for $j = 1, 2, \ldots, n_i$. Let Y_i

denote the $n_i \times 1$ longitudinal response vector for the ith subject, with element Y_{ij} denoting the value of the longitudinal outcome taken at time point t_{ij}. The distribution of Y_i is

$$Y_i \sim Negative\,binomial(\lambda_i, \lambda_i + \frac{\lambda_i}{\theta}^2)$$

- Mean: λ_i
- Variance: $\lambda_i + \frac{\lambda_i^2}{\theta}$,

where θ is the dispersion parameter. λ_i depends on the covariates via logarithmic link function as:

$$log\,(\lambda_i|b_i) = x_i^t\,(t)\,\beta\;(t) + z_i^T b_i = \eta_i\,(t)$$

$x_i\,(t)$ and $z_i\,(t)$ denote the design vectors for the fixed effects β and the random effects b_i, respectively. The random effects are assumed to follow a multivariate normal distribution with mean zero and variance-covariance matrix **D**.

The survival sub-model

For the survival process, we assume that the risk for an event depends on a function of the subject-specific linear predictor $\eta_i\,(t)$. More specifically, we have

$$h_i\,(t) = h_o\,(t)\,exp\{w_i^T\,(t)\;\gamma\;+ f\,\{\eta_i\,(t)\}\,\alpha\,\}$$

$h_0\,(t)$ denotes the baseline hazard function, $w_i\,(t)$ is a vector of exogenous, possibly time-varying, covariates with corresponding regression coefficients γ. Parameter vector α quantifies the association between features of the marker process up to time t and the hazard of an event at the same time point.

Parameters in the joint model were estimated under the Bayesian framework and implemented using Markov chain Monte Carlo (MCMC) methods. All statistical analyses were performed using R software, version 4.4.1 with JMBayes2 package at a significance level of 0.05. In order to address missing values in the dataset, we employed the MICE (Multivariate Imputation by Chained Equations) package.

Result

Descriptive result

The main dataset contained the information of 1028 patients, but the longitudinal CD4 measurements were not recorded for 273 patients. This data included an unbalanced longitudinal dataset. 755 HIV-positive patients with one or more CD4 measurements were included for statistical analysis. The frequency of CD4 measurements varied from 1 to 20 times over the follow-up period. The median age of patients was 34 years ($Q_1 - Q_3 =$ interquartile range (IQR) =11). The higher percentage of patients were male (67.8%). The median of baseline CD4 cells was 387 (IQR=411 cells/mm3). Follow-up times varied between individuals and in total, 6342 measurement occasions were available with a median number of visits per subject was 6 (IQR= 6). During the follow-up, 212 patients (28.0%) died 63.8% of patients have a history of unsafe sexual behavior, 33.2% of patients have a history of unsafe injection, 64.1% have a history of addiction, 58.6% of them were unemployed and, 6.1% have hepatitis B. 47.4% have been infected with this virus through injection addiction, 39.4% through sexual intercourse and 4.1% through mother-to-child transmission. The 1-year and 5-year survival rates are 91% (95%CI: 89%, 93%) and 79% (95%CI: 77%, 82%) respectively. More details about the demographic and clinical characteristics of the patients by the years from 2011 to 2016 are shown in Table 1.

Figure 1 shows an apparent non-linearity of the subject-specific CD4 count profiles for 63 randomly selected individuals. The Kaplan-Meier survival plots are shown in Fig. 2, females, employed individuals, and those without hepatitis B had a higher survival rate. The computation of age-standardized incidence and mortality rate (per 100000 population) is shown in Table 2. The incidence rate of HIV (per 100000 people) was reported by age group. The age-standardized mortality and incidence rates during the years 2011 to 2016 were 0.874 and 3.033 per 100,000 person-years respectively.

Joint model result

The effects of the various predictors on the hazard of death as well as the trend of CD4 cell count based on the joint model using the MCMC method were given in Table 3. (The level at which the parameter estimate was obtained is specified in parentheses in front of each variable). We examined the proportional hazards assumption and excluded the transmission way from the model because this assumption was not met.

We find a strong association between the CD4 cell count and the risk for death, with a unit decrease in the marker corresponding (Log(CD4)) to an exp(−(−1.7312)) = 5.64-fold increase in the risk for death. Table 3 represents the result of joint models. The risks of death are presented in Table 3 (a). Age was significantly associated with an increased risk of mortality ($P = 0.0052$). A history of addiction was associated with a higher risk of mortality ($P = 0.0568$). Additionally, patients with positive Hepatitis B results demonstrated a significantly increased risk of mortality (0.0458). The risk of death for men was exp(−(−0.1411)) = 1.27 times more than for women which is almost significant($P = 0.0604$).

The results of the longitudinal sub-model for the CD4 cell count are represented in Table 3 (b). The analysis of

Table 1 Demographic and clinical characteristics of patients in the study

Years	2011	2012	2013	2014	2015	2016	Total
No. of cases	110	144	159	132	167	43	755
No. of Death (Until 2022)	35	45	50	36	35	11	212(28.0%)
1-year survival (95% CI)	89% (83%, 95%)	94% (91%, 98%)	86% (81%, 92%)	91% (86%, 96%)	93% (90%, 97%)	91% (82%, 100%)	91% (89%, 93%)
5-year survival (95% CI)	78% (71%, 86%)	81% (74%,87%)	76% (69%, 83%)	78% (71%,85%)	84% (79%, 90%)	79% (68%, 92%)	79% (77%, 82%)
Age							
1st Qu.	27	29	28	30	30	34	29
Median	35	33	34	35	35	37	34
3rd Qu.	39	38	39	41	43	44	40
Gender							
Male	79	103	107	87	108	28	512(67.8%)
Female	31	41	52	45	59	15	243(32.2%)
Marital status							
Married	50	62	72	54	80	22	341(46.8%)
Single	59	82	86	76	87	20	410(53.0%)
Unknown	1	0	2	1	0	1	5(0.2%)
Educational level							
Diploma &less	103	132	151	121	182	36	695(92.0%)
Academic	5	10	7	6	7	3	38(5.0%)
Unknown	2	2	1	5	8	4	23(3.0%)
History of unsafe sexual behavior							
Yes	67	89	94	87	115	30	482(63.8%)
No	39	45	60	36	45	11	236(31.2%)
Unknown	4	10	5	9	7	2	37(5.0%)
History of addiction							
Yes	78	91	101	83	103	8	484(64.1%)
No	27	45	56	44	60	13	245(32.4%)
Unknown	5	8	2	5	4	2	26(3.5%)
History of unsafe injection							
No	9	17	17	11	20	5	79(10.4%)
Yes	47	48	54	47	44	10	250(33.2%)
Unknown	54	79	88	74	103	28	426(56.4%)
Result hbsag test							
Positive	8	8	11	5	11	3	46(6.1%)
Negative	85	123	133	110	140	36	627(83.0%)
Unknown	17	13	15	17	16	4	83(10.9%)
Job							
Employed	50	65	63	48	54	20	300(39.8%)
Unemployed	60	78	96	82	107	21	444(58.6)
Unknown	0	1	0	2	6	2	11(1.6%)
TransmissionWay							
Addiction	69	73	78	66	72	18	376(47.4%)
Sex	31	54	63	54	59	16	277(39.4%)
MotherToChild	3	9	4	4	9	0	29(4.1%)
Unknown	7	8	14	8	27	9	73(9.1)

longitudinal CD4 count measurements revealed that addiction was significantly associated with a decrease in CD4 count ($P<0.0001$). Age showed a marginally almost significant negative effect on CD4 count ($P=0.0616$) and being a man ($P=0.0358$) were associated with a decreased count of CD4 cells significantly.

Discussion

This research employed a Bayesian joint model to explore the relationship between the risk of mortality and the longitudinal changes in the CD4 biomarker, aiming to identify the factors influencing the survival of individuals infected with HIV. The joint model revealed a significant

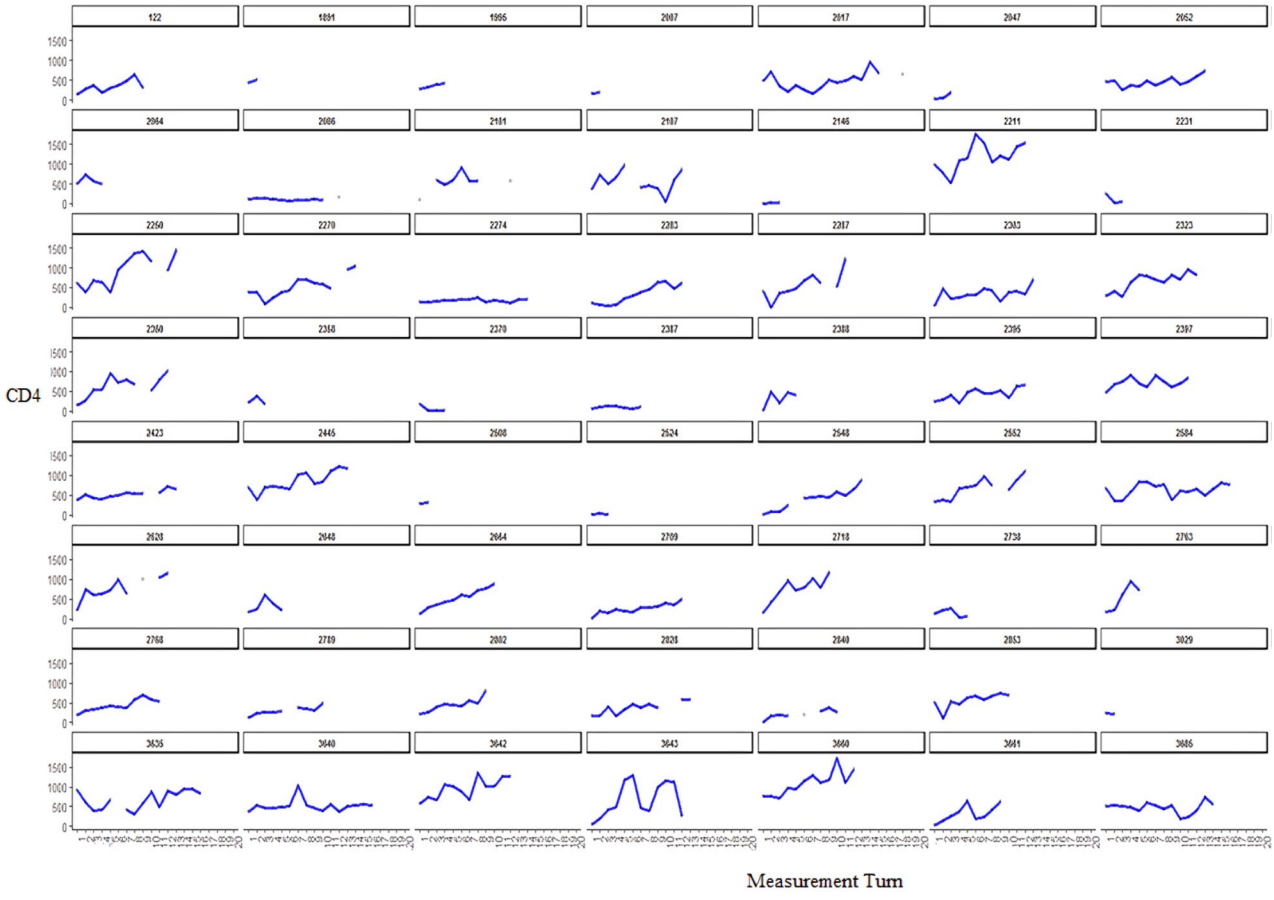

Fig. 1 CD4 trajectories of the CD4 measurements for a random sample of patients

correlation between CD4 cell counts and mortality risk, indicating that a one-unit decrease in the Log(CD4) is associated with a 5.64-fold increase in the risk for death. This finding aligns with a 2019 study conducted in North-West Ethiopia, which utilized joint latent class modeling to assess the survival of HIV-positive individuals based on CD4 cell counts and time-to-death [7]. They revealed that the risk of death hinged on longitudinal CD4 counts. In another study carried out in 2019 in Iran, the result show that the joint model provided a flexible framework for simultaneous studying of the effects of covariates on the level of CD4 cell count and the risk of progression to TB and AIDS. This model also assessed the effect of CD4 trajectory on the hazards of competing events [8].

According to the result of the joint model, in the survival sub-model: age, addiction and Hepatitis B, were statistically significant on the risk of death at a 95% confidence level. These results are in line with a study conducted in 2017 in Fars province in Iran, they used Time-varying Cox regression analyses, the findings of this study implied that some variables could play the role of risk factors in HIV patients, and shorten the patient's life span e.g. older age, female gender, unemployment, delay in HIV diagnosis, drug injection, and higher Hemoglobin levels [9].

Our finding indicates that age is associated with changes in CD4 cell counts over time. A study employing joint modeling techniques found that age, along with other factors such as weight and antiretroviral therapy adherence, significantly influenced the mean changes in CD4 cell counts in HIV patients [10]. Specifically, older age was associated with different trajectories in CD4 count progression, suggesting that aging may affect immune recovery during treatment. Age also plays a crucial role in determining mortality risk among HIV patients. The same study reported that older age was significantly associated with reduced survival time [10]. This finding underscores the importance of considering age as a factor when evaluating the prognosis of HIV-infected individuals.

According to our result of the joint model the risk of death was almost higher in males than females in as much as HIV-infected males were exp(-(-0.2411)) = 1.27 times at risk of death than HIV-infected females. This result is consistent with the results of a study conducted in 2019 [11] in which the risk of death in males was 5.145

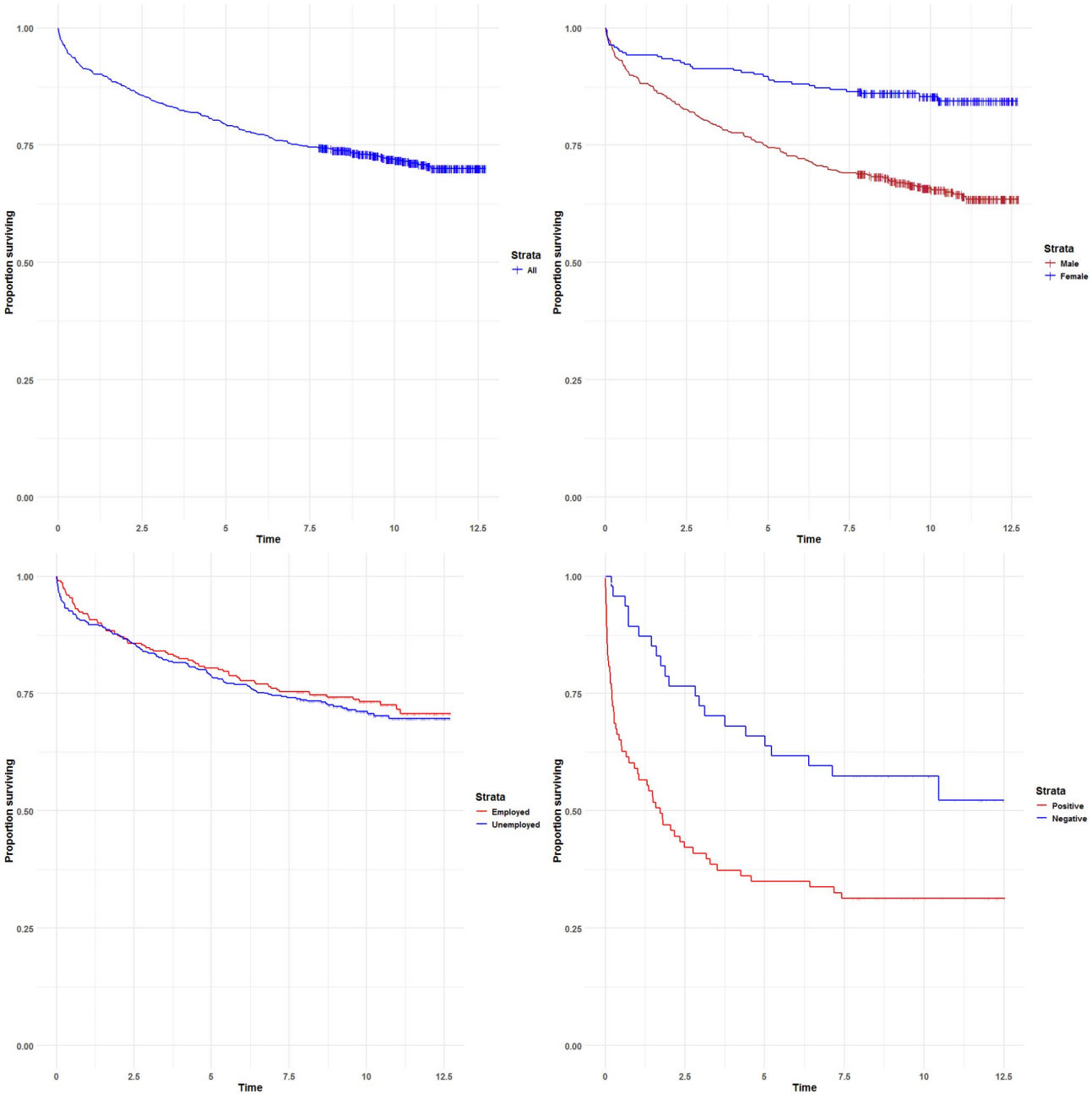

Fig. 2 Kaplan-Meier survival plot for the HIV/AIDS patients. The top-left graph shows the survival probabilities for all individuals. The top-right graph shows the survival probabilities stratified by gender (male and female). The bottom-left graph shows the survival probabilities for employed and unemployed individuals. The bottom-right graph shows the survival probabilities for individuals based on hepatitis B test results (positive vs. negative)

times the risk of death in females. Similarly, this result is in agreement with those observed in earlier studies [12]. In some studies the causes of shorter survival time in HIV-infected males versus females may be different, for instance, females in earlier stages may be more aware of their infection and take antiretroviral therapy. The findings derived from the present study align with those of prior investigations [13, 14].

In the longitudinal sub-model analyzing CD4 cell count, the variables of gender and addiction were found to be statistically significant at a 95% confidence level. Notably, gender emerged as a significant covariate influencing the longitudinal outcomes of CD4 cell counts, with females exhibiting a significantly higher CD4 count compared to their male counterparts. The results of this study are consistent with previous research [12, 15]. Gender is a critical determinant of HIV acquisition,

Table 2 Computation of age-standardized incidence and mortality rate (per 100000 population)

Age group	No. of cases	No. of death	Person at risk in 2011–2016 Fars province	Mortality rate Per 100,000 population	Incidence rate Per 100,000 population	Standard population WHO
[0–5)	17	3	1,915,000	0.156658	0.887728	88,569
[5–10)	10	1	1,765,000	0.056657	0.566572	86,869
[10–15)	2	0	1,660,000	0	0.120482	85,969
[15–20)	1	0	1,797,500	0	0.055633	84,670
[20–25)	41	4	2,315,000	0.172786	1.771058	82,171
[25–30)	106	27	2,710,000	0.99631	3.911439	79,272
[30–35)	183	44	2,455,000	1.792261	7.454175	76,073
[35–40)	177	48	1,912,500	2.509804	9.254902	71,474
[40–45)	99	36	1,565,000	2.300319	6.325879	65,876
[45–50)	58	24	1,342,500	1.787709	4.320298	60,378
[50–55)	28	10	1,142,500	0.875274	2.450766	53,681
[55–60)	22	11	950,000	1.157895	2.315789	45,484
[60–65)	8	3	697,500	0.430108	1.146953	37,186
Total	755	212	22,227,500	0.953773	3.396693	917,672

Table 3 The results of the joint modeling of longitudinal measurements (CD4 cell count) and time to event (death) for the all HIV/AIDS patients

Crude						Adjusted				
Variable	**Mean**	**StDev**	**2.5%**	**97.5%**	***P***	**Mean**	**StDev**	**2.5%**	**97.5%**	***P***
a) Survival Outcome										
Age	-0.0077	0.0048	-0.0195	-0.0009	0.0268	0.0319	0.0091	0.0214	0.0580	0.0052
Gender(Female)	-0.4023	0.2801	-0.9623	0.1282	0.142	-0.2411	0.3056	-0.7531	0.4629	0.0604
Unsafe Injection(Yes)	-0.1079	0.3513	-0.7664	0.6052	0.7536	-	-	-	-	-
Unsafe Sex(Yes)	-0.1932	0.2329	-0.6528	0.2527	0.4184	-	-	-	-	-
Addiction(Yes)	0.6767	0.2884	0.1189	1.2499	0.0166	0.5414	0.3216	-0.0864	1.1755	0.0568
Marital(Married)	-0.1321	0.2238	-0.5608	0.3148	0.5744	-	-	-	-	-
Education(Diploma &less)	-0.2694	0.6096	-1.4251	1.0130	0.6188	-	-	-	-	-
Job(Employed)	-0.2807	0.2281	-0.7125	0.1688	0.2214	-	-	-	-	-
Hepatitis B result(Positive)	0.5518	0.3939	-0.2729	1.2509	0.1724	0.5635	0.2941	-0.0183	1.1332	0.0458
Value(CD4)						-1.7312	0.2938	-2.2591	-1.1622	0.0000
b) Longitudinal Outcome										
Age	-0.0021	0.0008	-0.0036	-0.0005	0.0098	-0.0375	0.0249	-0.1038	0.0010	0.0616
Gender(Female)	0.3039	0.0524	0.2018	0.4060	0.0000	0.1621	0.0836	-0.0082	0.3179	0.0358
Unsafe Injection(Yes)	0.0112	0.1005	-0.1880	0.2078	0.9044	-	-	-	-	-
Unsafe Sex(Yes)	-0.0708	0.0556	-0.1815	0.0376	0.2016	-	-	-	-	-
Addiction(Yes)	-0.4006	0.0560	-0.5165	-0.2944	0.000	-0.3773	0.0697	-0.5263	-0.2671	0.0000
Marital(Married)	0.0746	0.0552	-0.0343	0.1813	0.1728	-0.0033	0.0474	-0.0880	0.0810	0.9948
Education(Diploma &less)	-0.2929	0.1134	-0.5124	-0.0676	0.0108	-0.0839	0.1176	-0.3444	0.1643	0.4026
Job(Employed)	-0.0717	0.0547	-0.1768	0.0387	0.1944	0.0744	0.0547	-0.0498	0.1735	0.1928
Hepatitis B result(Positive)	-0.1674	0.1201	-0.4054	0.0691	0.1674	-0.0650	0.1180	-0.2895	0.1985	0.5324

progression, and treatment outcomes. Women and men often experience different immunological responses, comorbidities, and social determinants of health, which can influence on HIV. Addiction is a significant factor in worsening health outcomes among individuals living with HIV. Studies have demonstrated that substance abuse can lead to impaired immune function and an increased risk of mortality. Previous studies using joint models have shown that addiction is associated with a reduction in CD4 cell count, which is a critical indicator of immune function in HIV patients and research has highlighted that persistent decreases in CD4 counts among individuals with substance use disorders correlate with a higher risk of mortality [8, 16]. Our study aligns with these findings, as we observed a significant decrease in the CD4 cell counts and an elevated mortality rate among HIV patients with a history of substance abuse. This further underscores the critical need to address addiction in the management of HIV.

In our joint model analysis, hepatitis B infection was found to significantly increase the risk of mortality among HIV patients. However, its effect on CD4 cell count in the longitudinal component of the model was not statistically significant. The risk of death for those with Hepatitis B was exp(0.5635) = 1.75 times that of those without hepatitis B. From a clinical perspective, hepatitis B increases the risk of AIDS or death in newly diagnosed patients, highlighting the importance of considering it as a significant risk factor for mortality in HIV patients, regardless of its impact on CD4 counts. The findings were in alignment with earlier studies [17, 18].

In this study, a joint model was used to analyze the longitudinal CD4 cell count and the survival time data. The association parameter between the longitudinal and survival components was statistically significant. This significance suggests a strong association between the CD4 cell count and the survival time of HIV patients. Patients with higher CD4 cell counts have better survival prospects compared to those with lower CD4 cell counts.

Previous studies have shown that joint models in contrast to separate models can lead to unbiased and more efficient estimates of parameters [19, 20]. The use of the joint model allows for a more comprehensive understanding of the factors influencing both the CD4 cell count and survival time, compared to using separate models. One notable limitation of this study is the absence of data regarding the antiretroviral therapy (ART) provided to the patients included in the analysis. This lack of information restricts our ability to fully understand the impact of ART on the outcomes observed.

Another limitation of this study is related to the selection of the time of HIV diagnosis as the baseline (time origin) for the analysis. While this approach allowed us to capture valuable longitudinal information on CD4 counts and other variables from the time of diagnosis, it does not account for the potential influence of ART initiation timing. Given the changes in ART initiation protocols over the past decade ranging from initiating ART only for CD4 counts below 300 or 500 to the current universal initiation immediately after diagnosis the timing of ART initiation varied significantly among participants in Iran. Using ART initiation as the time origin might have provided a more precise perspective on the effect of ART on CD4 trajectories. This limitation may affect the interpretation of CD4 trajectories, as ART initiation is known to significantly influence CD4 recovery. Consequently, our results likely reflect a combination of natural disease progression and the effects of ART, which could not be disentangled in this analysis. Without detailed ART data, covariate group differences in CD4 counts may also be confounded by differences in ART initiation timing, as individuals with lower CD4 counts might have initiated ART earlier according to WHO guidelines. Future studies incorporating comprehensive ART initiation data could build on our findings by explicitly modeling ART as a time-dependent covariate. This approach would allow for a clearer separation of ART effects from natural disease progression, improving the interpretability of CD4 trajectories. However, this choice would have resulted in the exclusion of critical data from the period between diagnosis and ART initiation, particularly for participants who began treatment years after diagnosis. Future studies with detailed and uniform ART initiation data could further explore this aspect to refine the understanding of CD4 progression in the context of ART. A Bayesian joint modeling approach enables individualized predictions of HIV progression and mortality by monitoring patients' CD4 counts [21]. It is also recommended that further studies that use the joint model for dynamic prediction on this data.

Conclusion

The joint model using the MCMC method revealed a strong association between CD4 cell count and the risk of death in HIV-infected individuals. The joint model offered a flexible framework for simultaneously examining the impacts of various factors on CD4 cell count levels and the risk of death. It also allowed us to evaluate the influence of CD4 trajectory on the risk of death in HIV patients. Decreased CD4 cell count was significantly associated with age, gender and addiction. Age and gender were positively associated with the risk of death, with men being at a higher risk. Hepatitis B was found to increase the risk of death. These findings align with previous studies on HIV-infected individuals.

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Author contributions
All the authors made substantial intellectual contributions to the study. S.Kh. supervised the whole research work, S.S.P. wrote, analyzed statistics, and interpreted results, M.N. data collection, Z.Sh. evaluated the research work and revised the writing of the manuscripts. All authors participated in editing the article. All authors approved the submission of this article. The authors read and approved the final manuscript.

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Data availability
The data supporting this study's findings are available from Shiraz University of Medical Sciences. Still, restrictions apply to the availability of these data, which were used under license for the current study. These data may be made available upon request, and are subject to a license agreement with Shiraz University of Medical Sciences; interested researchers should contact < mnejat91@gmail.com > to determine licensing terms.

Declarations

Ethics approval and consent to participate

This study utilized secondary data collected from the HIV/AIDS care system at Shiraz University of Medical Sciences. The collection of this data was conducted as part of routine care and treatment programs. Upon entry into these programs, verbal informed consent was obtained from all participants for the recording of their information. The verbal consent process was in accordance with the guidelines of the ethics committee at Shiraz University of Medical Sciences, which approved the use of this data for research purposes. This data was provided to the researcher without name, national code, address, and phone number. It only included variables used in the proposal, and we did not need to contact the participants. Permission to access data at this level was obtained through correspondence with the Shiraz University of Medical Sciences and university security approval. This study was performed in accordance with the Declaration of Helsinki and ethical approval was gained from the Shiraz University of Medical Sciences Ethics Committee (IR.SUMS.REC.1402.280). All study methods were performed in accordance with approved ethical guidelines and regulations throughout.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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