Longitudinal Systolic and Diastolic Blood Pressure Change over Time and Associated Risk Factors in Patients with Hypertension in Southwest Ethiopia: A prospective study

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Summary

BACKGROUND

Hypertension is a chronic disease that has a major health effect on adults and the elderly and is associated with increased risk of cardiovascular diseases and other morbidity. The objective of this study was to assess the factors that affect the longitudinal systolic and diastolic blood pressure change over time in hypertensive patients jointly.

MATERIALS AND METHODS

A prospective study design was employed using follow up records of hypertensive patients during a follow up time of 6 months. The data included 1,100 individuals with a minimum of two and maximum of six measurements per individual from February, 2019, and August, 2019. A joint model was considered to study the joint evolution and associated risk factors affecting the two end points.

RESULTS

Among all covariates included in joint models sex, age, diabetic mellitus, drinking coffee, drinking alcohol, chewing khat, physical exercise were significantly associated with systolic and diastolic blood pressure.

CONCLUSION

There is a strong positive association between the evolution of systolic and diastolic blood pressures. Hypertensive prevention should give stress on factors such as older age, diabetic mellitus, khat chewing, alcohol and coffee use during follow-up time.

***Key Words**: Joint Model, Systolic Blood Pressure, and Diastolic Blood Pressure*

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Introduction

Hypertension is a chronic disease that has a major health effect on adults and the elderly. It is defined as a persistent raised systolic or diastolic blood pressure equal to or more than 140/90 mmHg in adults aged 18 years and over [1, 2]. The evolution of blood pressure is linked to the adverse health outcomes of cardiovascular disease, stroke, and chronic renal disease. Approximately 7.6 million deaths and 92 million disability-adjusted life-years worldwide were attributable to high blood pressure in 2016 [3]. In Africa, hypertension is the main cause of the cardiovascular breakdown [4]. According to the Federal Ministry of Health report, in Ethiopia hypertension accounts for 1.8% of all deaths and the 7th leading cause of death in 2015 [5].

Monitoring hypertension is a necessity for patients to assess the evolution of blood pressure. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) are measured repeatedly over time after treatment to ensure no signs of blood pressure problems. These outcomes are needed to ensure an accurate evaluation of the blood pressure since they are correlated and could be influenced by the socioeconomic status and demographic characteristics of the patient [6]. Given the interdependence of these outcomes, it is important to evaluate the factors that affect the evolution of SBP and DBP in a joint manner [7].

When two outcomes are measured repeatedly, joint modeling is used in the context of jointly studying the time to clinical event and repeated measures on surrogate outcomes [8-11]. In resource-limited settings, joint modeling of SBP and DBP level in time is rarely scrutinized. Therefore, the foremost objective of this article was to identify factors that affect the longitudinal SBP and DBP change over time in hypertensive patients, jointly. In addition to assessing the factors that affect the SBP and DPB change over time, we were also interested in the association between the two endpoints measured simultaneously.

Materials and Methods

Study Design

We conducted a prospective follow-up study between February 01, 2019, and August 30, 2019, at Jimma University Medical Center (JUMC) hypertensive clinic.

Study Participants

The study included patients with hypertensive disorders who were enrolled in indirect observation during anti-hypertensive treatment during the study period.

Study Population and Sample Size

All hypertensive patients aged 18 years or older, who were coming to JUMC hypertension clinic for their regular follow up during periods of February 01, 2019, and August 30, 2019, were eligible for this study. Patients with two and more than two observations were included in the analyses leading to a total of 1100 patients and 4400 observations. Patients' follow up time was one month apart, according to the doctors' orders. The duration between the initial and the last recorded visits ranged from one to six months.

Study Variables

The study had two outcome variables which was systolic and diastolic blood pressures, whereas the independent variables that were used to explain the outcome variables were age, sex, educational status, alcohol consumption, smoking cigarettes, chewing khat, physical exercise, drinking coffee, diabetes mellitus and family history of hypertension.

Data Collection

A structured administered questionnaire was used to collect the data related to socio-demographic characteristics and a checklist was used to collect data related to clinical variables from physical examination findings such as SBP, and DBP. A baseline survey of demographic and clinical variables (age, sex, educational status, smoking cigarette, chewing khat, physical exercise, drinking coffee, diabetes mellitus, and family history of hypertension) was conducted at the first visit of taking treatment. The above-mentioned study variables were rechecked when patients came to the hypertensive clinic for drug collection. During the intensive phase, which was the first month of hypertensive treatment, patients came to the clinic for direct observation treatment on Monday or Wednesday.

During the continuous phase, which was between the second and sixth months of treatment, patients were taking anti-hypertensive drugs from the clinic every month. SBP and DBP were measured in mmHg during the initiation of antihypertensive drugs as a baseline and repeatedly measured per month. To assure the data quality, two health professionals for data collection and one supervisor were assigned. Training was given regarding the study objectives and data collection process for data collectors and supervisors for one day.

Data Collection Instrument and Procedure

Blood pressure was measured using a mercury sphygmomanometer and stethoscope. A patients' systolic and diastolic blood pressure was taken while the patient was in a sitting position, from the right arm after the patients were asked to rest for at least 5 minutes before measurement. If they were taking any caffeinated beverages, they were asked to rest for 30 min. Three consecutive measurements of blood pressure on a single visit were taken at least 5 minutes apart, and the averages of the three records used for the computation of results. The point at which the first Krokoff sound was heard was taken as SBP, and the DBP was taken to be the point at which the sound disappeared [12].

Data Analysis

Joint modeling enables researchers to study several outcome variables simultaneously. Joint modeling of such kind of data is necessary to quantify, the relationship between evolutions of different responses. The joint modeling approach investigated in this study was the bivariate longitudinal mixed effect models that included both fixed and random effects.

The joint model investigated the link between change in SBP and DBP measurement, that is, the association of changes. Several authors modeled the bivariate mixed effect to investigate the joint evolution of two longitudinally measured outcomes. Studies [13-15] have recently been published on joint mixed effect models for longitudinal outcomes Systolic blood pressure (SBP) and diastolic blood pressure (DBP) of hypertensive patients and Heart Rate (HR) or Pulse Rate (PR) and Respiratory Rate (RR) of congestive heart failure patients, respectively. To analyze, this data the standard statistical packages are available in several software particularly, freely accessible software R, which is good to model the linear mixed effect model easily handling intra-subject correlation [16].

Thus, the two longitudinally measured outcomes of vector $Y_i(t)$, at each occasion which is designed in below are supposed to be modeled jointly.

Suppose the vector $Y_i^k=\begin{bmatrix} \text{SBP}_i \\ DBP_i \end{bmatrix}$ be the response vector for the individual i , with SBP_i and DBP_i having n_i sampled measurements of the marker k (k = 1, 2), hence possibly proposed model for joint longitudinal continuous outcomes data with assumption of Gaussian process is

$$SBP_i = \mu_1(t) + a_{1i} + b_{1i} + \varepsilon_{1i}(t)$$
$$DBP_i = \mu_2(t) + a_{2i} + b_{2i} + \varepsilon_{2i}(t) \quad (1)$$

Where, $\mu_1(t)$ and $\mu_2(t)$ refer to the population means at time t.

Both response trajectories are tied together through a joint distribution for the random effects.

$$\begin{bmatrix} a_{1i} \\ b_{2i} \\ a_{2i} \\ b_{2i} \end{bmatrix} \sim MVN(0, G) \quad (2)$$

Where, the variance-covariance matrix for the random effects, G, has the following structure: $G=\begin{bmatrix} \sigma_{a1}^2 & \sigma_{a1b1} & \sigma_{a1a2} & \sigma_{a1b2} \\ & \sigma_{b1}^2 & \sigma_{b1a2} & \sigma_{b2b1} \\ & & \sigma_{a2}^2 & \sigma_{a2b2} \\ & & & \sigma_{b2}^2 \end{bmatrix} =$

$$\begin{bmatrix} 131.654 & -11.542 & 81.542 & 7.652 \\ & 2.785 & 7.010 & 0.730 \\ & & 53.661 & -1.942 \\ & & & 0.355 \end{bmatrix} \quad (3)$$

The SBP is associated with the evolution of DBP is typically derived from the covariance matrix of the random effects. Indeed, the correlation between both evolutions is given by:

$$\text{AE}= \frac{Cov(b_1,b_2)}{\sqrt{Var(b_1)}\sqrt{Var(b_2)}} = \frac{\sigma_{b_1 b_2}}{\sqrt{\sigma_{b_1}^2}\sqrt{\sigma_{b_2}^2}} \quad (4)$$

Variables with a p-value<0.05 were considered as the associated risk factors for the evolution of SBP and DBP. Though many demographic variables and clinical factors were considered in the analysis, only covariates significantly associated with SBP and DBP were reported.

Ethics approval and consent to participate

Ethical clearance was obtained from the Research and Post Graduate Office of Jimma University, College of Natural science. Written permission to conduct the study was granted by the JUMC. The study was reviewed and approved by the Jimma University, College of Natural Science Research Ethics Committee and Jimma University Medical Center Patient's Ethics Committee. During a face-to-face visit, research assistants explained study objectives to each prospective participant.

Results

Out of the total of 1100 adult hypertensive patients, 558(51%) were females and 469(42.6%) were between 18 and 49 age groups. Mean age at the start of follow up was 51.34 years (SD=13.41 years) with 623(57%) of them living in an urban area (Jimma town), and 371(37%) having attended elementary school.

Among the study participants, 521(42%) had a family history of hypertension, 456(41.5%) patients had diabetic mellitus, 644(58.5%) patients had no other related disease and 393(35.7%) were cigarette smokers. Out of all, 406(37%) were drinking alcohol frequently, 578(52.5%) were drinking coffee, 280 (25.5%) of patients were chewing khat, and 487(44.3%) of the respondents were exercising regularly (Table 1).

Table 1 Baseline Socio-Demographic and Clinical factors of Patients with Hypertension in JUMC, February 01, 2019 to August 30, 2019

Variable	No. (%)	Percentage (%)
Age		
18–49	469	42.6
50–65	468	42.5
> 65	163	14.8
Gender		
Male	542	49
Female	558	51
Place of residence		
Urban	623	57
Rural	477	42
Family history of hypertension		
Yes	521	42
No	579	58
Diabetes mellitus		
Yes	456	41.5
No	644	58.5
Education level		
Illiterate	352	29
Elementary	371	37
Secondary	178	16
Higher education	199	18
Smoking cigarette		
Yes	393	35.7
No	707	64.3
Chewing khat		
Yes	280	25.5
No	820	74.5
Drinking coffee		
Yes	578	52.5
No	522	47.5
Alcohol consumption		
Yes	406	37
No	694	63
Physical Exercise		
Yes	487	44.3
No	613	55.7

The mean SPB and DBP of patients declined at time=0 to the next 6 months period during follow up time. The baseline SBP mean of patients was 141.10(SD=18.91) mmHg and declined to 130.41(SD=18.87) mmHg over time and similar history was found in DBP mean of patients (Table 2).

Table 2 Summary Statistics of outcome variables measured per months at Follow-Up time in JUMC, February 01, 2019, to August 30, 2019

Time in month	SBP			DBP		
	Mean(SD)	Min-Max	95%CI	Mean(SD)	Min-Max	95%CI
0	141.10(18.91)	80-240	139.61-142.59	87.02(12.45)	40-160	86.05-87.99
1	138.15(17.26)	80-230	136.92-139.39	85.24(12.58)	60-140	84.37-86.11
2	136.74(17.5)	90-210	135.55-137.94	83.59(10.43)	40-120	82.75-84.43
3	135.14(17.68)	70-220	133.87-136.43	83.03(12.48)	40-130	82.97-85.10
4	134.00(19.23)	80-200	132.45-135.56	82.71(13.12)	50-120	81.64 -83.78
5	130.41(18.87)	89-210	128.39-132.44	82.23(12.79)	40-130	80.93-83.52

Exploring Individual Profile Plots for SBP and DBP over time

The longitudinal outcomes, SBP and DBP, were measured at irregular time intervals with one a month's gap. The variability of SBP between individuals was higher at baseline and appeared to decrease through time. Likewise, there was between and within subject's variability in DBP. In general between and within subject specific differences could not be ignored. Further, the average profiles of SBP and DBP had linear relationships over time which were decreasing, but with different evolution through time (see figure 1 below).

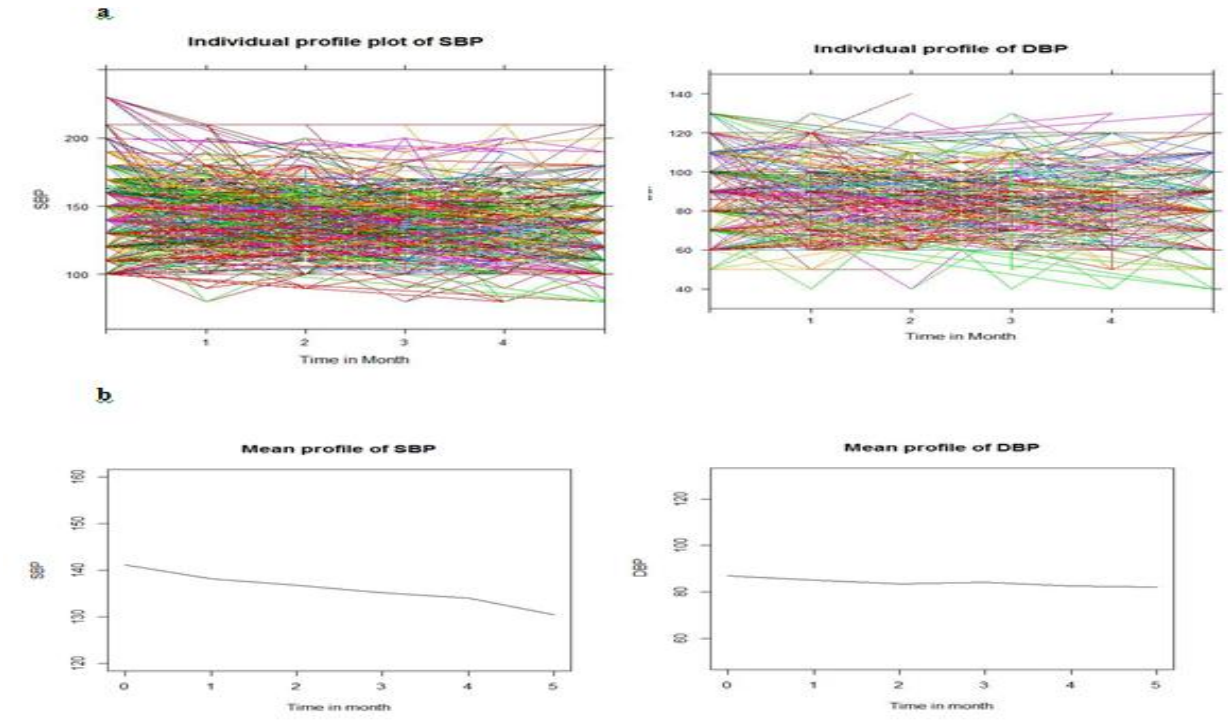

Figure 1(a) Individual Profile and (b) Mean Profile Plots for SBP and DBP of Hypertensive Patients in JUMC, February 01, 2019 to August 30, 2019

Joint Analysis of Systolic and Diastolic Blood Pressure

A joint linear mixed-effects model (1) was used to fit the DBP and SBP, assuming an unstructured variance-covariance structure. This model is the same as the separate model except the random intercepts and slopes for SBP and DBP were correlated rather than independent. It was fitted allowing for a linear time effect for each covariate and by considering significant covariates as a fixed effect with all possible interaction terms.

Among all covariates sex, age, drinking coffee, drinking alcohol, chewing khat, physical exercise, were significantly associated with both outcomes, but place of residence, family history of hypertension, smoking cigarette, and education level were statistically insignificant with SBP and DBP. Thus, the insignificant terms were removed from the model and refitted. After removing the insignificant terms, the AIC value dropped from 30865.4 to 30694.6 indicating a better fit.

Table 3: Parameter Estimates and Standard Errors for the Joint Model of the SBP and DBP Outcomes in JUMC, February 01, 2019 to August 30, 2019

SBP				**DBP**			
Parameters	**Estimates**	**S.E**	**P-V**	**Parameters**	**Estimates**	**S.E**	**P-V**
Constant	136.95	2.901	0.001*	Constant	84.22	1.821	0.000*
Sex	1.83	1.142	0.001*	Sex	2.351	0.302	0.017*
Age	2.032	1.200	0.032*	Age	0.225	1.015	0.036*
Diabetes mellitus	0.521	0.032	0.001*	Diabetes mellitus	0.474	0.603	0.004*
Drinking Coffee	1.133	0.012	0.002*	Drinking Coffee	1.185	0.006	0.039*
Alcohol consumption	1.045	0.258	0.001*	Alcohol consumption	1.103	0.120	0.019*
Chewing Khat	2.803	0.305	0.002*	Chewing Khat	1.024	0.005	0.001*
Physical Exercise	-0.241	0.009	0.030*	Physical Exercise	-0.114	0.105	0.031*
Time	-0.144	0.054	0.006*	Time	-0.234	0.231	0.002*
Age ×Time	1.324	0.301	0.000*	Age ×Time	-0.104	0.512	0.012*
Coffee × Time	2.819	0.201	0.011*	Coffee × Time	0.103	0.006	0.022*
Khat ×Time	0.012	0.010	0.001*	Khat ×Time	1.156	0.126	0.623
Exercise×Time	-0.231	0.009	0.030*	Exercise×Time	-0.214	0.006	0.001*
Random Effects							
$Var(a_{10i})$	131.654			$Var(a_{20i})$	52.213		
$Var(b_{11i})$	2.785			$Var(b_{21i})$	0.355		
$Corr(a_{10i}, b_{11i})$	-0.812			$Corr(a_{20i}, b_{21i})$	-0.443		
σ_1^2	152.285			σ_2^2	84.112		

** indicates significance at 0.05 level of significance AIC value=30694.6*

Table 3 presents the fixed-effect intercept coefficient SBP=136.95 (S.E. = 2.901) represents an estimate of the average of SBP at time=0 excluding all covariates in the model. Likewise, the fixed-effect intercept coefficient DBP=84.22 (S.E. =1.821) represents an estimate of the average of DBP at time=0 and excluding all covariates in the model.

Among all covariates sex, age, diabetes mellitus, drinking coffee, alcohol consumption, chewing khat were positively associated with both outcomes (P-value <0.05). There was also evidence that age had positive effect on evolution of SBP (Age=2.032; S.E. =1.200) and on DBP (Age=0.225; S.E. = 1.015). Sex was significantly associated with both SBP and DBP outcomes. Female patients had 1.83 (S.E. =1.142) mmHg higher over the evolution of SBP and 2.351 (S.E. =0.302) mmHg DBP compared to males. Likewise, diabetes mellitus was significantly associated with both SBP and DBP outcomes; diabetes patients have 0.521(S.E=0.032) mmHg higher over the evolution of SBP and 0.474 (S.E. =0.603) mmHg DBP compared with non-diabetic patients.

Similarly, drinking coffee was significantly associated with both SBP and DBP, thus, patients drinking coffee had 1.133mmHg higher over the evolution of SBP and 1.185mmHg higher over the evolution of DBP when compared to counterparts. In the same way, Alcohol consumption had a positive effect on the SBP (Alcohol consumption =1.045; S.E. = 0.258; P-value< 0.001) and on the DBP (Alcohol consumption =1.103; S.E. =0.0002; P=<.0001). This indicates alcohol users had 1.045 mmHg higher over the evolution of SBP and 1.103 mmHg higher evolution of DBP when compared to non-users.

Chewing khat was also significantly associated with both SBP and DBP, thus, patients chewing khat had 2.803 mmHg higher over the evolution of SBP and 1.024 mmHg higher over the evolution of DBP when compared to non-users. However, physical exercise had a negative effect on the SBP with (physical exercise =-0.241; S.E. = 0.009; P-value< 0.030) and on the DBP with (Physical exercise =1.024; S.E.=0.005; P=<.0001), this indicates patients with exercise had lower changes in 0.241 mmHg of SBP and 1.024 mmHg lower evolution of DBP when compared to non-exercise patients.

Time–age interaction was also significantly and positively associated with SBP (Age×Time = 1.324(0.301); P=0.000) and significantly and positively associated with DBP (Age×Time =0.104(0.0004); P<0.012). Similarly time-drinking coffee had a positive effect on the SBP (Coffee × Time=2.819; S.E=0.201) and on the DBP (Coffee × Time=0.103); [S.E. =0.00019]; P=<.0001).

In a similar way, chewing khat-time interaction was also significantly and positively associated with SBP (Khat ×Time=0.012; S.E. =0.010, p<0.0001) and but there was no significant association with DB (P-value >0.05). Likewise time-physical exercise interaction had a negative effect on the SBP (Exercise ×Time =-0.231; S.E=0.009) and on the DBP (Exercise ×Time = -0.214; S.E=0.006, P=<.001).

The parameter estimate for time was negatively associated with both SBP (Time= -0.144; S.E=0.054) and DBP (Time=-0.234; S.E=0.231). This indicates a unit increase in time was associated with 0.144mmHg decrease on SBP, and 0.234mmHg decrease on DBP; after adjusting for other covariates.

Generally, as it is indicated in the results in Table 3, both SBP and DBP have a decreasing pattern throughout the follow up with respective clinical treatments. This concept indirectly indicated the improvement in the risk of hypertensive patients because the lower value of both symptoms SBP and DBP is directly related to a stronger and healthier heart.

The intercept of the random effects for both SBP and DBP indicates there is variability between subjects at baseline. And the slope of random effects for both SBP and DBP indicates there is variability within subjects over time.

The correlation -0.812 and -0.443 indicates, there is a negative correlation between intercept and slope of linear time effect for the random part for SBP and DBP, respectively. In addition, from the random effects, the residual terms σ12 =152.285 and σ22 =84.111 indicates that variation within the hypertensive patients in different time of SBP and DBP measurements, respectively.

Association between the Two End Points

SAS PROC MIXED [17] for joint model provides the estimated variance covariance matrix for random effects of both the SBP and the DBP as determined in the form of using equation (3) above. The association between the random intercept for the SBP and DBP can be determined by using equation (4), which is AE $=\frac{Cov(b_1 b_2)}{\sqrt{Var(b_1)}\sqrt{Var(b_2)}} = \frac{0.7301}{\sqrt{2.785}\sqrt{0.355}}$ =0.7342. The larger positive value indicates there is positive strong association between the evolution SBP and DBP.

Discussion

This study described the link between systolic and diastolic pressure in hypertensive patients. In addition, the study identified predictors for systolic and diastolic pressure among patients who were taking anti-hypertensive drugs.

Before fitting the joint model of two out comes, data analysis was explored to identify general trends within subjects that could detect change over time thus providing information about the variability at given times. From individuals profile plot, we observed the existence of variability in both SBP and DBP within and between individuals. The exploratory analysis result for mean structure suggested that on average, both SBP and DBP measures slightly decreasing. This supports the results of Tomeckova and Stanovska [18], who found that the average values of BP in hypertensive patients at the end of the study was lower compared to the entry.

Results of the joint model in this study suggested that a strong positive association between the evolutions of SBP and DBP. This result is supported by Edwards and Fisher [19] who showed a strong association between repeated systolic and diastolic BP outcomes.

This finding is also similar to a study done by Thorp [20] which showed that there is a strong association between the evolutions and a slowly increasing evolution of the association between DBP and SBP over time for children aged two through eighteen years. Furthermore, the additional information gained by incorporating information about the correlations between the responses was able to reduce the variability in both the fixed-effects estimates as well as the random-effects estimates. Such result is consistent with the previously published data on hypertensive patients' blood pressure measurements using semi-parametric mixed model [21].

In this study all the covariates and their interaction term by time were considered, of these sex, age, drinking coffee, drinking alcohol, chewing khat, time and the interaction terms age by time, drinking coffee by time, chewing khat by time and physical exercise by time were significantly associated with an increasing of SBP and DBP through time. In this regard, the findings from separate analyses of longitudinal SBP and DBP by Oliveria *et al*., [22] who found that among socio-demographic variable sex, age, drinking coffee, drinking alcohol, chewing khat, time and the interaction terms age by time, stress by time and physical exercise by time were significantly related with hypertension, supports these results.

Place of residence, family history, educational status and marital status were not significant. The association of SBP and DBP with the covariates sex, age, drinking coffee, smoking cigarette, and chewing khat was consistent with other studies [23–24].

The result of this study revealed that there is an association between systolic and diastolic blood pressure at baseline and during follow-up among patients with diabetes. This result was similar to a study in the Louisiana State University Hospital-based longitudinal data [25–26], and blood pressure at baseline and during follow-up and the risk of all-cause mortality among patients with diabetes [27]. A similar study conducted at Felege Hiwot Referral Hospital, Bahir Dar, Ethiopia also showed that there is an association between blood pressure at baseline and during follow-up among patients with diabetes [23].

In the current study, SBP among female patients was significantly higher than male patients; this is consistent with the results from other studies [28-29]. The reason for this difference could be the impact of the geographic zone, earlier puberty in girls than boys, and as a result the elevated BP in girls due to puberty hormones.

The finding showed that alcohol consumption is a major risk factor to elevate the systolic and diastolic blood pressure of hypertensive patients. Alcohol users had 1.045 points higher over evolution of SBP and 1.103 points higher over evolution of DBP when compared to non-users. This finding is similar to studies done in Gonder [30], Deber Markos [31], and Addis Abeba [32]. The possible explanation is that alcohol increases stimulation of sympathetic nervous system, endothelin, insulin resistance and inhibition of vascular relaxing substances which leads to hypertension. According to the general facts of alcohol and hypertension states regularly drinking alcohol increase substantially the risk of developing hypertension. Therefore, persons should reduce alcohol intake especially for those risk groups like cardiac problems, liver problems, and other chronic co-morbid diseases.

In this study, patients with drinking coffee history had raised SBP and DBP than patients with hypertension who were not drinking coffee. The study also identifies that patients who drank coffee were associated with increasing SBP and DBP than patients who did not drink coffee.

Furthermore, our study found that patients chewing khat had increased SBP and DBP than patients with hypertension who were not chewing khat. This result is coherent with a study done by Kiber *et al*.,[31] and Helelo *et al*.,[33], who stated that chewing khat is the leading cause of death in patients with hypertension.

This study also showed that physical exercise had a negative effect on the SBP and DBP; indicating patients with physical exercise had 0.241 points lower over evolution of SBP and 1.024 DBP when compared to non-exercise patients. This result was consistent with the study conducted in southern Ethiopia and northwest Ethiopia [33]. This is due to the fact that, physical exercise decreases the SBP and DBP in the risk of hypertension [34].

In this study older age patients with hypertension were associated with higher SBP and DBP than younger adult patients; this is consistent with the findings of another study [35]. It appears that the increase in cardiac mass with aging results in the increase of blood pressure levels in older age groups. Similarly, another study identified higher SBP and DBP among older patients with hypertension than those who were younger [35]. Another similar study found that the odds of having hypertension

among older age (age greater than 50) were three times more likely compared to those younger. [36]. Perhaps this could be because persons with relatively older age could be affected by other non-communicable diseases.

The presence of family history of previously diagnosed hypertension did not have any association on the change of both SBP and DBP. Some of the findings from joint linear mixed model by Chenglin et al., [37] support these results. They identified age and previously diagnosed hypertension to be positively associated with change in SBP, but sex was insignificant for SBP. They found age to be negatively associated with change in DBP, but sex and previously diagnosed hypertension were positively associated with change in DBP.

Conclusion and Recommendations

The joint mixed effect model with unstructured variance-covariance structure was preferred among others to fit the DBP and SBP. It can be generalized that there is a strong positive association between the evolutions of SBP and DBP. Thus, joint modeling of the two responses, incorporates all information simultaneously and provides valid and efficient inference with better accuracy. Therefore, fitting joint model is recommended.

The baseline mean of the two outcomes was out of the normal range for hypertensive patients but it declines through clinical treatment follow-up time of 6 month period intervals. Hypertension prevention and control strategies should give emphasis on factors such as female sex, older age, diabetic mellitus, coffee users, alcohol users, and khat chewers during follow-up time. Regular physical exercise decreases the evolution of SBP and DBP. Therefore, health care providers should focus on the above modifiable risk factors to reduce the evolution of SBP and DBP hypertensive patients.

Limitations

The main limitation to joint modeling is the inherent computational and a number of technical challenges that arise from the increasing dimensionality of the random effects component.

Operational Definitions

- Alcohol consumptions: - the consumption of local or manufactured alcoholic beverages greater than 30 gram of ethanol per day
- Cigarette smoker: - smoking any pack of cigarette
- Family history of hypertension:- Hypertension status among blood relatives (Father, Mother and Grandfather and grandmother).
- Diabetics mellitus: - Diabetics status among hypertensive patients
- Physical exercise:-Walking, jogging, swimming and cycling at least 30 minutes per day
- Chewing Khat: - Regular khat chewers' individuals who reported chewing for 5 days or more in a week

Abbreviations

AE: Association of the evolution; AIC: Akaike Information Criteria; BIC: Bayesian Information; Criteria; DBP: Diastolic Blood Pressure; JUMC: Jimma University Medical Center; LMM: Linear Mixed Effects Models; MOH: Minister of Health; SAS: Statistical Analysis System; SBP: Systolic Blood Pressure; SD: Standard Deviation; SE: Standard Error; WHO: World Health Organization.

Consent for Publication

Not required

Availability of Data and Study Materials

The data sets analyzed in this study are available from the corresponding author upon a reasonable request.

Competing interests

The authors declare that there is no conflict of interest associated with the material presented in this study.

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Authors' Contributions

All authors (YN, AD, RH and FZ) conceived, designed and conducted the study, analyzed the data, contributed materials/analysis tools and wrote the paper.

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Reference

1. **Mills KT, Bundy JD, Kelly TN, Reed JE, Kearney PM, Reynolds K, Chen J, He J.** Global disparities of hypertension prevalence and control: a systematic analysis of population-based studies from 90 countries. *Circulation*. 2016 Aug 9; 134(6):441-50.
2. **Forouzanfar M, Liu P, and Roth G**. Global burden of hypertension and systolic blood pressure of at least 110 to 115 mm hg, 1990-2015. *Jama*. 2017; 317:165–82.
3. **Chockalingam A, Campbell NR, Fodor JG.** Worldwide epidemic of hypertension. *Can J Cardiol*. 2006; 22(7):553.
4. **Miura K, Nagai M, Ohkubo T.** Epidemiology of hypertension in Japan. *Circulation Journal*. 2013; 77(9):2226–31.
5. **Tibazarwa K, Damasceno A.** Hypertension in developing countries. *Can J Cardiol*. 2014; 30(5):527–33.
6. **Abebe S, Berhane Y, Worku A, Getachew A**. Prevalence and associated factors of hypertension: a cross-sectional community based study in Northwest Ethiopia. *PLoS ONE*. 2015;10(4):e0125210.
7. **Asfaw L, Ayanto Y, Gurmamo FL**. Hypertension and its associated factors in Hosanna town, Southern Ethiopia: community based cross-sectional study. *BMC Res Notes*. 2018;11(1):306.
8. **Asresahegn H, Tadesse F, Beyene E**. Prevalence and associated factors of hypertension among adults in Ethiopia: a community based cross-sectional study. *BMC Res Notes*. 2017;10(1):629.
9. **Bonsa F, Gudina E, Hajito K.** Prevalence of hypertension and associated factors in Bedele Town, Southwest Ethiopia. *Ethiop J Health Sci*. 2014;24(1):21–6
10. **Tesfaye F.** Epidemiology of cardiovascular disease risk factors in Ethiopia: the rural-uban gradient (Doctoral dissertation, Epidemiologi och folkhälsovetenskap), 2008.
11. **Gibbons R, Hedeker D, DuToit S.** Advances in analysis of longitudinal data. *Annu Rev Clin Psychol*, 2010;6:79–107.
12. **Hypertension control.** Report of a WHO Expert Committee. *World Health Organ Tech Rep Ser*. 1996;862:1–83
13. **Fieuws S, Verbeke G.** Joint modeling of multivariate longitudinal profiles: pitfalls of

the random-effects approach. *Stat Med*. 2004;23(20):3093–104.
14. **Fieuws S, Verbeke G**. Pairwise fitting of mixed models for the joint modeling of multivariate longitudinal profiles. B*iometrics*. 2006; 62(2):424–31.
15. **Neupane B, Beyene J** Bivariate linear mixed model analysis to test joint associations of genetic variants on systolic and diastolic blood pressure. *BMC.* 2014, 8: S75.
16. **Davey, D. and MacGillivray, I.** (1988). The classification and definition of the hypertensive disorders of pregnancy. *American journal of obstetrics and gynecology*, 158(4):892–898.
17. **Littell RC, Milliken GA, Stroup WW, Wolfinger RD Schabenberger O.** SAS system for mixed models. *Journal of Biopharmaceutical Statistics*; 17:2, 363-365.
18. **Tomeckova, M. and Stanovská, Z**. Control of hypertension and survival analysis of the hypertensive patients in Stulong - longitudinal study of risk factors of atherosclerosis, Proceedings of MIE2003. IOS Press; 2003.
19. **Edwards, L., Fisher, M., Wolfinger, R., Qaqish, B. and Schabenberger, O.** An R statistic for fixed effects in the linear mixed model, Statistics in Medicine**;** 2008; **27**, 6137-6157
20. **Thorp, J.** "Joint Mixed-Effects Models for Longitudinal Data Analysis: An Application for the Metabolic Syndrome." (2009).
21. **Binod N., Joseph B.** Bivariate linear mixed model analysis to test joint associations of genetic variants on systolic and diastolic blood pressure. *BMC proceeding.* 2014; 8
22. **Oliveria, S, Lapuerta, P, McCarthy, B. Asch SM**. Physician-related barriers to the effective management of uncontrolled hypertension. 2000; **162**:413–420.
23. **Workie DL, Zike DT, Fenta HM.** Bivariate longitudinal data analysis: a case of hypertensive patients at Felege Hiwot Referral Hospital, Bahir Dar, Ethiopia. *BMC Research Notes*. 2017 Dec 1;10(1):722.
24. **Amare B., Tilahun T, Yihun M, Ermias M, Endalew W, Saba A,Tewabech T, Yezibalem M and Getasew T**. Prevalence and associated factors of hypertension among adult patients in Felege-Hiwot Comprehensive Referral Hospitals, northwest, Ethiopia: a cross-sectional study. *BMC Res Notes* .2018; 11:876
25. **Zhao W, Katzmarzyk P, Horswell R, Wang Y, Johnson J, Cefalu W, et al**. Blood pressure and stroke risk among diabetic patients. J Clin Endocrinol Metab. 2013;98(9):3653–62.
26. **Zhang Y, Li W, Wang Y, Chen L, Horswell R, Xiao K, et al.** Increasing prevalence of hypertension in low-income residents within Louisiana state university health care services division hospital system. ***Eur J intern Med***. 2012;23(8):e179–84.
27. **Li W, Katzmarzyk PT, Horswell R, Wang Y, Johnson J, Hu G.** Blood pressure and all-cause mortality among patients with type 2 diabetes. ***Int J Cardiol***. 2016;1:206
28. **Opie H, Seedat Y.** Hypertension in sub-Saharan African populations. ***BMC Cardiovasc Disord***. 2005;112(23):3562–8.
29. **Asresahegn H, Tadesse F, Beyene E.** Prevalence and associated factors of hypertension among adults in Ethiopia: a community based cross-sectional study. ***BMC Res Notes***. 2017;10(1):629.
30. **Awoke A, Awoke T, Alemu S, Megabiaw B.** Prevalence and associated factors of hypertension among adults in Gondar, Northwest Ethiopia: a community based cross-sectional study. ***BMC Cardiovasc Disord***. 2012;12(1):113.
31. **Kiber M, Wube M, Temesgen H, Woyraw W, Belay YA.** Prevalence of hypertension and its associated factors among adults in Debre Markos Town, Northwest Ethiopia:

community based cross-sectional study**.** ***BMC research notes.*** 2019 Dec 1;12(1):406.

32. **Angaw K, Dadi F, Alene A.** Prevalence of hypertension among federal ministry civil servants in Addis Ababa, Ethiopia: a call for a work place screening program. ***BMC Cardiovasc Disord***. 2015; 15(1):76.
33. **Helelo T, Gelaw Y, Adane A**. Prevalence and associated factors of hypertension among adults in Durame Town, Southern Ethiopia. ***PLoS ONE***. 2014;9(11):112790.
34. **Anteneh Z, Yalew W., Abitew D.** Prevalence and correlation of hypertension among adult population in Bahir Dar city, northwest Ethiopia: a community based cross-sectional study. ***Int J General Med***. 2015;8:175.
35. **Bonsa F, Gudina E, Hajito K.** Prevalence of hypertension and associated factors in Bedele Town, Southwest Ethiopia. E***thiop J Health Sci.*** 2014;24(1):21–6
36. **Asfaw L, Ayanto Y, Gurmamo FL.** Hypertension and its associated factors in Hosanna town, Southern Ethiopia: community based cross-sectional study. ***BMC Res Notes.*** 2018;11(1):306.
37. **Chenglin Y, Foster G, Kaczorowski J, Chambers LW, Angeles R, Marzanek-Lefebvre F, Laryea S, Thabane L, Dolovich L.** The impact of a cardiovascular health awareness program (CHAP) on reducing blood pressure: a prospective cohort study. *BMC public health*. 2012 Dec 1;13(1):1230