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Risk Factors for Change Blood Pressure Through Time: A Hospital Based Study

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ABSTRACT

Background: Adults and elderly are particularly affected by hypertension, a chronic condition that raises the risk of cardiovascular disease and other morbidities. This study aimed to evaluate the variables that influence how longitudinal changes in systolic and diastolic blood pressure occur in hypertension individuals.

Methods: The follow-up data of hypertension patients were used in a prospective research design throughout a 6-month follow-up period. The data comprised 1,100 people between Feb and Aug 2019 with a minimum of two and a maximum of six measures per subject. A joint model was considered to investigate how the two end points joint evolution and related risk variables impact them.

Results: Sex, age, diabetes mellitus, drinking coffee, drinking Alcohol, smoking khat, and physical activity were substantially linked with systolic and diastolic blood pressure among all factors included in joint models.

Conclusion: Systolic and diastolic blood pressure changes have a significant positive correlation. During the follow-up period, hypertensive prevention should emphasise variables such as advanced age, diabetes mellitus, khat chewing, alcohol usage, and coffee use.

Key-words: Blood pressure, Chronic hypertension, Diastolic, Systolic, Joint models

INTRODUCTION

Chronic hypertension affects individuals and elderly negatively in terms of their health. It is described as a persistently elevated systolic or diastolic blood pressure in individuals 18 years of age and older that is equal to or more than 140/90 mmHg [1,2]. Blood pressure changes are related to the unfavourable effects of cardiovascular disease, stroke, and chronic kidney disease on health.

In 2016, high blood pressure accounted for 7.6 million fatalities and 92 million disability-adjusted life years globally [3].

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The primary contributor to cardiovascular disease in this place is hypertension [4]. In India, hypertension was the seventh-highest cause of death in 2015, accounting for 1.8% of all fatalities, according to data from the Federal Ministry of Health [5].

Patients must monitor their hypertension to gauge how their blood pressure is changing. After therapy, systolic and diastolic blood pressure are periodically checked to make sure there are no indicators of blood pressure issues. Due to their correlation and potential effect on the patient's socioeconomic situation and demographics, these results are required to assess blood pressure appropriately [6]. Given the interdependence of these results, it is crucial to determine the variables that influence the development of Systolic blood pressure (SBP) and diastolic blood pressure (DBP) together [7].

Joint modelling is employed in jointly examining the time to clinical event and repeated assessments on surrogate

outcomes when two outcomes are examined frequently [8–11]. Joint modelling of SBP and DBP levels in time is rarely explored in resource-constrained contexts. Consequently, the main goal of this paper was to pinpoint variables that influence how longitudinal SBP and DBP vary over time. A group of patients with hypertension. We were interested in the connection between the two endpoints assessed concurrently and the variables that influence the SBP and DPB change over time.

MATERIALS AND METHODS

Study Design- Between February 1 and August 30, 2019, we performed prospective follow-up research at the hypertension clinic at PRM Medical College, Baripada.

Study Participants- We conducted a prospective follow-up study at the PRM Medical College, Baripada, hypertension clinic between February 1 and August 30, 2019.

Study Population and Sample Size- The study's participants were all hypertensive patients, age 18 or older, who visited the hypertension clinic for their routine follow-up between February 1 and August 30, 2019. The analyses comprised patients with two or more observations, totaling 1100 individuals and 4400 observations. The doctors prescribed a one-month interval between patient follow-up appointments. One to six months passed between the first and last documented visits.

Study Variables- Systolic and diastolic blood pressures were the study's two outcome variables, and age, sex, educational level, alcohol use, cigarette smoking, gutkha chewing, physical activity, coffee consumption, diabetes mellitus, and family history of hypertension were used as independent variables to explain the outcome variables.

Data Collection- Data on socio-demographic parameters were gathered using a structured administered questionnaire, and data on clinical variables from physical examination findings, such as SBP and DBP, were collected using a checklist. At the first visit to receive therapy, a baseline survey of demographic and clinical factors (age, sex, educational status, smoking, chewing khat, physical activity, drinking coffee, diabetes mellitus, and family history of hypertension) was completed. When patients visited the hypertension clinic to pick up their medications, the study variables were evaluated again. Patients visited the clinic for direct observation therapy on Mondays or Wednesdays during the intense phase, the first month of hypertension medication. Patients used anti-hypertensive medicines from the clinic once a month throughout the continuous phase of therapy, which was between the second and sixth months of care. SBP and DBP were routinely checked monthly after baseline measurements were taken when anti-hypertensive medication was started. Two health experts for data collection and one supervisor were appointed to ensure the data quality. Data collectors and supervisors received one day of training on the study's goals and data-gathering procedure.

Data Collection Instrument and Procedure- Blood pressure was measured using a mercury sphygmomanometer and stethoscope. After being instructed to relax for at least five minutes, a patient's systolic and diastolic blood pressure was obtained from the right arm while the patient was seated. They were instructed to take a break if they consumed any caffeinated beverages. For 30 minutes, the findings were calculated using the averages of three blood pressure readings collected on consecutive days at least five minutes apart. The SBP was determined to be the location of the initial Krokoff sound, and the DBP was determined to be the location of the sound's disappearance [12].

Analysis of Data- Researchers were examined many outcome factors simultaneously thanks to joint modelling. The link between the evolutions of various reactions must be quantified, which requires joint modelling of this data type. The bivariate longitudinal mixed effect models with both fixed and random effects were the joint modelling strategy examined in this study. The combined model examined the relationship, or association, of changes between SBP and DBP measurements. Some writers have modelled the bivariate mixed effect to investigate how two longitudinally observed outcomes have changed together. Recent studies [13–15] on joint mixed effect models for longitudinal outcomes SBP, DBP, & heart rate (HR) or pulse rate (PR), as well as respiratory rate (RR), have been published.

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Standard statistical programmes, including R (free and open-source software), are readily available to analyse this data and are particularly useful for modelling the linear mixed effect model and addressing intra-subject correlation [16].

Thus, the two longitudinally measured outcomes of vector $Y_i(t)$, at each occasion designed below, should be modelled jointly.

Suppose the vector $Y^k=[^{SBP_i}_{DBP_i}]$ 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

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

Where $\mu_1(t)$ and $\mu_2(t)$ refer to thepopulation means at time t.

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

$$[^{a_{1i}}_{b_{2i}}] \sim MVN(0, G)$$

2i

b_{2i}

(2)

Where the variance-covariance matrixfor the random effects, G, has the following

$$\sigma^2 \quad \sigma_{a1b1} \quad \sigma_{a1a2} \quad \sigma_{a1b2}$$

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

Ethics approval and consent to participate- The Jimma University College of Natural Science's Research and Post Graduate Office provided ethical approval. The JUMC gave its written consent for the study to be carried out. The Jimma University College of Natural Science Research Ethics Committee and the Jimma University Medical Centre Patients' Ethics Committee examined and approved the study. A research assistant gave Each potential volunteer a personal explanation of the study's goals.

RESULTS

Table 1 described about the Baseline Socio-Demographic and Clinical factors of patients with Hypertension disease in JUMC, during the period of February 01, 2019 to August 30, 2019.

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 Female	542	49
	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

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

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

Time (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 (Fig. 1).

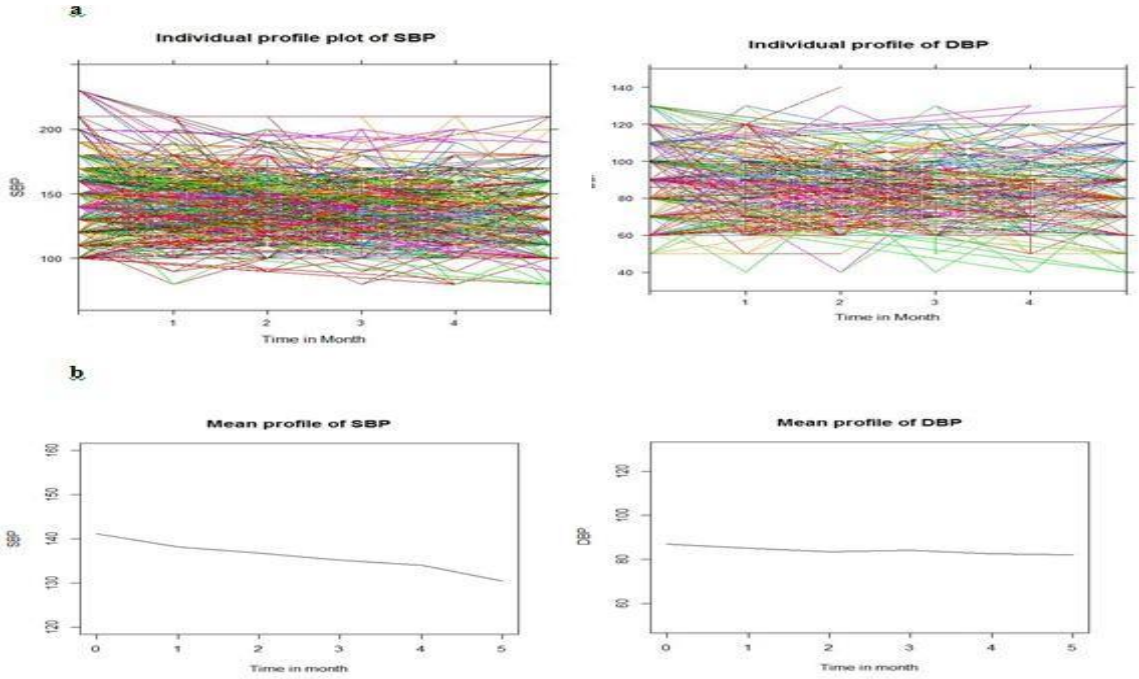

Fig. 1(a): Individual Profile and **(b)** Mean Profile Plots for SBP and DBP of Hypertensive Patientsin JUMC, February 01, 2019 to August 30, 2019

Joint Analysis of Systolic and Diastolic Blood Pressure- Under an unstructured variance-covariance structure, a joint linear mixed-effects model (1) was employed to fit the DBP and SBP. The only difference between this and the separate model is that the random slopes and intercepts for SBP and DBP were correlated rather than independent. It was fitted by considering all potential interaction terms, considering significant covariates as a fixed effect, and allowing for a linear temporal product for each covariate.

SBP and DBP were strongly influenced by all factors, including sex, age, drinking coffee, drinking Alcohol, smoking cigarettes, and chewing khat. Still, location of residence, family history of hypertension, smoking, and education level had no statistically significant impact on either outcome. Thus, the model was revised and the irrelevant terms were eliminated. The AIC value decreased from 30865.4 to 30694.6 when the unrelated words were eliminated, showing an improved match.

The average SBP at time=0 is estimated using Table 3 fixed-effect intercept coefficient SBP=136.95 (S.E.= 2.901), which omits all model variables. Like the DBP estimate, the fixed-effect intercept coefficient DBP=84.22 (S.E. =1.821) excludes all model variables and estimates the average DBP at time=0.

Table 3: Parameter Estimates and Standard Errors for the Joint Model of the SBP and DBPOutcomes 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*
guthkha ×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		
1				2			
σ^2	152.285			σ^2	84.112		

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

DISCUSSION

Association between the two end points, the estimated variance-covariance matrix for random effects of both the SBP and the DBP, as derived in the form of using equation (3) above, is provided by SAS PROC MIXED [17] for the joint model. Equation (4), the results of Tomeckova and Stanovska [18], who observed that the average values of BP in hypertension patients after the trial were lower than the entrance, may be used to assess the connection between the random intercept for the SBP and DBP. The combined model's findings in this study indicated a considerable positive correlation between the development of SBP and DBP. The findings of Edwards *et al.* [19], who demonstrated a high correlation between recurrent systolic and diastolic BP outcomes, lend credence to this conclusion.

This conclusion is also consistent with research by Thorp [20], which demonstrated a significant relationship between the evolutions of DBP and SBP throughout time for children between the ages of two and eighteen years. Additionally, the additional knowledge acquired by including data on correlations between the replies decreased the which reads AE = Cov(b1,b2). Variability in both the fixed and random-effects estimates, Var(b1) Var(b2) = 0.7301 2.785 0.355. As a result, =0.7342. The greater positive value shows the stronger positive correlation between the development of SBP and DBP.

This research discussed the relationship between systolic and diastolic pressure in hypertension. In addition, the study found predictors for both systolic and diastolic pressure among individuals on anti-hypertensive medications. Data analysis was investigated before fitting the combined model of two outcomes to find broad patterns among individuals that might detect change over time and provide details about the variability at specific moments. We could see from the individual profile plot that there was variation in SBP and DBP within and between people. The results of the exploratory analysis for mean structure indicated that both SBP and DBP measurements were generally somewhat declining. This backs up is in line with previously reported findings on semi-parametric mixed model blood pressure measures of hypertensive individuals [21].

All covariates and their interactions with time were considered in this study, including 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 activity by time.

These covariates were all significantly related to an increase in SBP and DBP over time. In this regard, Oliveria *et al.* [22] findings from separate analyses of longitudinal SBP and DBP show that sex, age, drinking coffee, drinking Alcohol, smoking khat, time, and the interaction terms age by time, stress by time, and physical activity by time were significantly associated with hypertension among socio-demographic variables. Residence, family history, level of education, and marital status were not important factors. It was consistent with prior research [23,24] that SBP and DBP were related to age, sex, drinking coffee, smoking cigarettes, and chewing gutkha.

According to the study's findings, there is a correlation between baseline and follow-up systolic and diastolic blood pressure among diabetic patients. This outcome was consistent with research based on longitudinal data from the Louisiana State University Hospital [25,26], and blood pressure at baseline and throughout follow-up and the risk of all-cause death among diabetes patients [27]. An identical study at Felege Hiwot Referral Hospital in Bahir Dar, Ethiopia, revealed a correlation between baseline and follow-up blood pressure levels in diabetic patients [23].

SBP was considerably greater in female patients in the current research than in male patients, which is consistent with the findings of prior studies [28,29]. The geographic zone's influence, girls' earlier onset of puberty than boys', and the higher blood pressure brought on by puberty hormones in girls might all contribute to this discrepancy. The results demonstrated that drinking Alcohol significantly increases hypertension individuals' systolic and diastolic blood pressure. Alcohol users showed higher SBP and DBP evolution scores than non-users by 1.045 and 1.103 points, respectively. This result is consistent with research from Awoke *et al.* [30] and Kiber *et al.* [31]. Alcohol may enhance insulin resistance, endothelin stimulation, vascular relaxing agents' inhibition, and sympathetic nervous system activation, which results in hypertension. Considering the common information about Alcohol and Alcohol use regularly significantly raises the risk of hypertension states. Therefore, people should limit their alcohol use, especially if they fall into risk categories like those with heart issues, liver issues, or other chronic co-morbid disorders.

In this study, individuals with hypertension who had a history of consuming coffee had higher SBP and DBP than patients with hypertension who did not. The study also shows that patients who drank coffee had higher SBP and DBP than those who did not. Additionally, our research revealed that patients eating khat had higher SBP and DBP than hypertensive individuals who were not chewing khat. The findings of this study are consistent with those of the study by Kiber *et al.* [31], which found that chewing khat is the primary cause of mortality in people with hypertension. This study also shown that physical activity had a detrimental impact on SBP and DBP, with patients who engaged in physical activity having SBP over time that was 0.241 points lower and DBP that was 1.024 points lower than those who did not.

CONCLUSIONS

To fit the DBP and SBP, the joint mixed effect model with an unstructured variance-covariance structure was chosen above the alternatives. A substantial positive correlation between the evolutions of SBP and DBP can be said to exist in general. Therefore, combined modelling of the two replies combines all available information concurrently and offers accurate and reliable inference. Consequently, it is advised to use a suitable joint model. The two outcomes' baseline means were outside of the hypertensive patients' normal range, but they started to fall after 6-month intervals of clinical therapy follow-up.

During the follow-up period, hypertension prevention and management efforts should focus on characteristics such as female sex, older age, diabetes mellitus, coffee, Alcohol, and khat users. Regular exercise slows the progression of SBP and DBP. Therefore, healthcare professionals should concentrate on the modifiable risk factors to slow the progression of SBP and DBP hypertensive patients.

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