Joint Longitudinal Data Analysis in detecting Predictors of Hypertension and Type2 Diabetes among adults receiving treatment at Felege Hiwot Teaching and Specialized Hospital, North-western Ethiopia

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Research article

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Abstract

Background Hypertension is one of the chronic diseases with major health problems over the centuries due to its significant contribution to the global health burden. It is familiar that the hypertensive patients are also exposed to other diseases like diabetes in which the two are highly associated to each other. The objective of current investigation was to identify longitudinal predictors of hypertension and type2 diabetes for adult patients receiving treatments at Felege Hiwot Teaching and Specialized Hospital, North western Ethiopia.Methods In this study, 748 hypertensive and type2 diabetic adult patients were randomly selected using systematic sampling technique. A retrospective longitudinal study was conducted on the selected patients to identify predictors of hypertension and type2 diabetes. Patients were receiving treatments related to both hypertension and type2 diabetes.Results The current investigation revealed that age and weight of patients were positively and significantly associated with existence of hypertension and type2 diabetes whereas; visiting times were negatively associated with development of the two response variables. Rural patients, patients who are smoking, drinking alcohols and patients with family disease history were joint predictors for existence variables of interests. The interaction of visiting times * sex, visiting times *residence area and age *sex of patients were also significant factors for the existence of response variables.Conclusion Hypertensive patients living in rural areas and those who are drinking and smoking were highly affected by the existence of type2 diabetes. Awareness should be created to those hypertensive and type2 diabetic patients to attend properly their treatment as prescribed by the health staff. They should also be advised to checkup their hypertension (systolic/ diastolic) and diabetes of type2 regularly.

Background

Hypertensive and type2 diabetes are two common persistent conditions that have significant impacts on health care systems in both the developed and developing world [1]. Previous study conducted in the USA indicates that the existence of type2 diabetes was about 2.5 times more likely in hypertensive persons than in their normotensive counterparts [2]. The two associated diseases, as most important parts of the metabolic syndrome, often co-exist, and lead to a aggravation in cardiovascular prognosis [3]. Majority of adult population are affected with hypertension which is highly correlated to stroke, ischemic heart disease and the like [4].

Effective strategies to prevent type2 diabetes in people with hypertension are urgently needed, especially in countries with a high population prevalence of hypertension [5]. Hypertension is a chronic and risk factor for the development of a number of disease progression [6, 7]. The development of hypertension is powerfully related with cardiac and vascular abnormalities that can be harmful for other important parts of the body like heart, kidney brain and other organs of the body [1]. The development of hypertension is used to diagnoses whether or not a person is experiencing high blood pressure [8].

A hypertensive and type2 diabetic patient visits a hospital in order to follow up the amount of systolic/diastolic blood pressures and the amount of glucose concentration in the blood. Systolic blood pressure is the amount of pressure that blood exerts on vessels while the heart is beating. If only the top number is greater than 140 mm Hg, the individual has a situation of isolated systolic blood pressure. On the other hand, the diastolic blood pressure is the amount of blood pressure on the bottom reading that is occurred when the heart is comfortable. For hypertensive patients, the average systolic reading is higher than 140 mm Hg and the average diastolic reading is greater than 90 mm Hg [11, 12]. For hypertensive individuals, the small blood vessels in the very important organs are most affected over time. These blood vessels become scarred, toughened, and less elastic, and this further leads to organ damage or failure. In a hypertension reading, for instance 120/80, it is the number on the top for systolic and a number on the bottom for diastolic. If the top and bottom blood pressures are both very high, a person is in a situation to have high blood pressure/hypertension. On the other hand, diabetes of type2 is the amount of fasting glucose concentration in their blood.

Therefore, maintaining a normal blood pressure is a very important component of reducing the risk of a heart attack, stroke or organ damage. The existence of very high value for both top and bottom reading indicates that a person is in a situation of hypertension and is associated with other related diseases such as coronary heart disease, diabetes of type2, etc. Socio-demographic and clinical covariates can affect for the development of hypertension and existence of type2 diabetes for individuals affected by two diseases namely hypertension and type2 diabetes. The joint random-effects are more flexible to identify correlation patterns between hypertension and for the development of type2 diabetes [9-11].

Previously, studies were conducted to identify factors influenced only two responses like systolic blood pressure(SBP) and diastolic blood pressures(DBP) [12, 13]. Longitudinal measurements on continuous or discrete response with time to event are commonly conducted for each subject[14]. Similarly, a number of studies have been conducted to identify variants associated with single blood pressure (BP) measures: systolic blood pressure (SBP), diastolic blood pressure (DBP), or a linear function of them [14]. However, there are controversies from the findings obtained from the previous studies [9-11]. Therefore, the objective of current investigation was to identify joint predictors of hypertension and type2 diabetes for both hypertensive and diabetic type2 patients who were getting treatment at Felege Hiwot Teaching and Specialized Hospital, north western Ethiopia. To the best of our knowledge, there is a scarcity of previous studies conducted to identify joint predictors of two longitudinal and inter related outcomes receiving treatment in the study area. Previous researchers recommended that, joint modeling gives more efficient inference than separate analyses given that the interest is drawing joint inference about the similar or different outcomes [15, 16].

It is our firm belief that statistically significant interaction effects of the two outcomes obtained in current investigation have practical contribution by giving insight to complex and advanced theories with the application to one of the critical problems in life science and public health practitioners.

Methods

Study Design

Institution based retrospective cohort study was conducted on 748 hypertensive and diabetic type2 patients at Felege Hiwot teaching and specialized hospital, North-Western Ethiopia, with original purpose of follow up/ check up the amount of blood pressure and fasting glucose concentration in the blood.

Source of data: The data used to current investigation were secondary data obtained at Felege Hiwot Specialized and Teaching Hospital.

Eligibility Criterion: Both hypertensive and diabetic type2 patients, 18 years or older and had follow ups between September 2015 and August 2017 with at least three visits for each patient were eligible for this study. A total of 748 patients who met the eligibility criteria and who had repeated measures of hypertension and type2 diabetes were retrospectively recorded from patients' medical follow up card by trained health workers in the hospital.

Reason for selection of study area: The study area was selected because of its high number of patients receiving treatment by qualified health care providers with full laboratory equipments, and it is a teaching and specialized hospital that is providing organized hypertension and related diseases follow up treatments. In addition, the hospital is one of the referral hospitals in the region with computerized data base system.

Variables under current investigation

Response variables: Patients' hypertension reading and amount of fasting glucose concentration in the blood measured repeatedly at each follow up visits were considered as a response variables. The diagnosis of type2 diabetes was conducted by the endocrinologists according to the fasting venous blood glucose concentration (tested with Glucose Oxidase Method) and the presentation of clinical outcomes of diabetes of type2 was leveled based on the 1999 World Health Organization criteria [15]. The hypertension (high reading values on the top and bottom components) was also tested by qualified health staff at each visiting time of patients. This was conducted for both hypertensive and diabetic type2 patients at each follow up visits freely.

The hypertensive status (systolic blood pressure [SBP]/diastolic blood pressure [DBP]):120/80 mmHg for the normal group; 120–139/80–89 mmHg for the pre-hypertension group; 140–159/90–99 mmHg for the stage 1 hypertension group; and 160/100 mmHg for the stage 2 hypertension group [9-11]. On the other hand, a study conducted using 75-g oral glucose tolerance test (OGTT), diabetes was defined as a fasting glucose concentration of 126 mg/dL or a post load glucose concentration of 200 mg/dL after the 75-g OGTT based on the World Health Organization criteria [15].

Covariates (independent variables): Age in years, weight in kg, smoking status (yes, no), drinking status (yes, no), consumption of meat (never, rarely, frequently), consumption of vegetables (never, rarely, frequently), physical exercise (never, rarely, frequently), residence area (rural, urban), sex (male, female), family disease history for hypertension or type2 diabetes (yes, no), follow ups visits, marital status (living with partner, living without partner), level of education (illiterate, primary, secondary and above), and chewing chat (yes, no).

Modeling joint outcomes: Suppose a sequence of longitudinal measurements , j = 1, 2, ..., , i = 1, 2, ...,n and k= 1,2 which represent the jth observation, from the ith subject, for the kth response variable. The linear mixed-effects model for each response variable on subject i taken at time t can be defined as:

$$\begin{cases} Y_{i1}(t) = \mu_{i1}(t) + W_{i1}(t) + \varepsilon_{i1}(t) \\ Y_{i2}(t) = \mu_{i2}(t) + W_{i2}(t) + \varepsilon_{i2}(t) \end{cases}$$

Where $W_{i1}(t) = a_{i1}(t) + b_{i1}(t)$, $W_{i2}(t) = a_{i2}(t) + b_{i2}(t)$, $\mu_{i1}(t)$ *and*, $\mu_{i2}(t)$ represent for the average result, a_{i1} and a_{i2} and $b_{i1}(t)$ *and* $b_{i2}(t)$ represent individual/subject specific random intercepts and random slopes respectively. The random intercept and random slopes can describe how the subject specific profiles deviate from the average profile for the two outcomes. ε_{ik}(t), where k = 1,2 is error term.

Linear mixed effect model often used in the literature for modeling a longitudinal continuous outcomes and provides a general and flexible modeling framework based on a random effects approach[17].

The classical approach to inference is based on estimators obtained from maximizing the marginal likelihood function [18, 19]. A logistic regression model was used to check whether or not missingness were affected by previous results and this indicated that dropouts were independent of the previous outcomes (χ_1^2= 0.2418, p-value = 0.354).

Results

The baseline characteristics of patients are indicated in Table 1. Table 1 shows that 362(44.4%) of the patients were females, 523 (69.9%) were lived in rural area, 236 (31.6%) were living without partner and the rest were living with partner. Among the patients, 145 (19.4%) were smokers and the rest were non-smokers. Similarly, among the total respondents, 215 (28.7%) were chewing chat and the rest were not. More than half (56.3%) of the respondents were not drinking alcohol. Regarding physical exercise, among the patients, 252 (33.7%) did not make any physical exercise, 296 (39.6%) of them did their exercise rarely and the rest did their exercise regularly or frequently. Table1 also indicates that, the majority of the patients, 358(47.9%) were frequently meat eaters and the majority of them were rarely vegetarians. Regarding the family disease history, 245 (32.8%) had family disease history for any one of the two diseases.

As it is indicated in Table1, continuous predictors were also recorded and the average age of patients was 57 years old, average weight of all patients was 64 kg and the average height of patients was 1.5 meter. The baseline characteristics of dependent variables were registered and indicated in Table1. Table1 indicates that the average hypertension was 146/95mmHg and average fasting glucose concentration was 132mg/dL.

Both the fixed and random components of the model were selected using Akakai Information Criteria (AIC) and Bayesian Information Criteria (BIC). Among the random effects, fixed effect + random intercept and random slope had the smallest AIC and BIC; hence, it has been selected as a random effect that should be included for current investigation.

In current investigation, model building was started from single covariate analysis approach. To do this, first a single covariate analysis was conducted to screen out potentially significant variables in the multi covariate model.

The joint model was performed to hypertension and type2 diabetes. In order to fit the joint model of the two response variables namely, hypertension and type2 diabetes, linear mixed models were considered separately for parameter estimation for marginal models as shown in Table2 and then conditional random effects models were developed (Table3). Finally, parameter estimation for linear predictor of hypertension for the response variable, type2 diabetes was constructed as shown in Table4. The main and significant interaction effects of the joint model for two outcomes are also indicated in Table4.

Table2 indicates that; age, weight, sex, residence area, smoking status, drinking status and visiting times were statistically affected the two response variables. Similarly, among the interaction effects visiting time *sex, Age*sex, visiting time * residence area were significantly affected the variable of interests.

Table2 indicates that; age, weight, sex, residence area, smoking status, drinking status and visiting times were statistically affected the two response variables. Similarly, among the interaction effects; visiting time *sex, Age*sex, visiting time * residence area were significantly affected the variable of interests.

The separate model indicated in Table2 was univariate distributions. Table3, on the other hand, indicates the combination of the separate models of hypertension and type2 diabetes by having presence joint multivariate distribution on the random effect. The analysis was done using likelihood function with Laplace approximation. The conditional independence of random-effect models considered in this analysis indicates that the LMM approach can be extended to multivariate longitudinal data by assuming separate random effect for each outcome and combining them by having presence a joint distribution on the random effects.

The SAS procedure using identity link function allowed us to impose the joint distribution on the random effects from the two separate models.

The conditional independence random intercept model in Table3 indicates that age, weight, physical exercise, family disease history, smoking status, drinking alcohol status, and visiting time were statistically significant for the two responses. On the other hand, the interactions effects like visiting time with sex, age with sex, and visiting time with residence area significantly affected the variable of interests.

In Table3, the same sign in parameter estimation indicates for positive correlation between the two responses. The conditional independence approach shown in Table3, failed to converge for overall model, as conditional independence assumption might be restrictive. Introducing conditional dependence of one response interims of the other using linear predictor is helpful in this case, which is used to validate the observed correlation rising from the random intercepts of the two response variables[20]. Hence, constructing a linear mixed model for hypertension and type2 diabetes variables including hypertension in the linear predictor is important for solving the problem of convergence as indicated in Table4.

As shown in Table4, age, weight, hypertension, physical exercise, sex, residence area, family disease history, smoking status, drinking alcohol status, marital status, chewing chat and visiting times significantly affected the progression rate of type2 diabetes. Hence, as age of a patient increased by one year, the amount of fasting glucose concentration in the blood increased by 0.65 mg/dL (95% CI: (0.03, 0.98), p-value <0.01). As weight of patients increased by one kg, the amount of fasting glucose concentration in the blood also increased by 0.71 mg/dL (95% CI: (0.04, 0.99), p-value < 0.01) keeping the other variables in the model constant.

Similarly, as patients' hypertension increased by one unit, the amount of fasting glucose concentration in blood also increased by 0.67 mg/dL (95% CI :(0.03, 0.95), p-value < 0.01). As visiting time of a patient increased by one unite, the amount of fasting glucose concentration in blood of patients decreased by 0.38 mg/dL (95% CI: (-3.45, -0.54), p-value = 0.03).

The amount of fasting glucose concentration in the blood of rural patients was smaller than that of urban patients. Comparing smokers with that of non-smokers, the amount of fasting glucose concentration in the blood of non-smokers was smaller than that of smokers. The repeated measures of average amount of fasting glucose concentration in the blood of non-alcoholic consumers were smaller than alcoholic consumers. Similar to main effects some interaction effects were also significant in Table4. Some of the significant interaction effects are the following.

a) **Interaction Effects between visiting time and sex of patients:** The results in Table4 and Figure1 indicated that as visiting time increased by one unit, the amount of fasting glucose concentration in the blood of female patients decreased by 0.36 mg/dL compared to male patients given the other variables constant. Therefore, the smaller variation gap in variable of interest between males and females observed at the beginning of the follow-up period increased with increase of the number of follow-up visits.

Discussion

In the current investigation, certain covariates were significantly and jointly affected the two responses namely, hypertension and type2 diabetes. As age of a patient increased, the three responses were also increased but the rate of increase for female and male patients were different. Hence, as age increased by one year, the average increasing rate of hypertension and type2 diabetes for female patients were smaller as compared to male patients. This result is in agreement with the previous researches[9, 21]. Weight of patients affected the two responses jointly and positively and this result also agreed with previous research [22]. As visiting time of patients increased by one unit, the amount of the two responses decreased. The possible reason for this may be results of successive treatment reduce the amount of hypertension and type2 diabetes. However, the rate of reduction for female patients was greater than that of male patients [15]. One of the potential reasons might be females had good experience in taking pills for family planning and this experience leads for good adherence of treatment for the two responses. Females have more exercises in home for preparing/cooking foods as compared to males and this may be another reason for their differences. As visiting time of patients increased by one unit, the rate of reduction for urban patients was greater than rural patients. This result is similar to previous research[12]. One of the potential reasons for this is that urban patients may follow seriously their treatment giving attention for their checkup after initiation of adherence. Urban patients give more attention for follow up of their health status in better way as compared to rural patients.

Conclusions

From the joint mixed effects model of hypertension with type2 diabetes patients, the covariates such as sex, age, smoking status, drinking status, visiting times of health institutions were significantly associated with the variable of interests. Among the interaction effects of the variable of interests, age and weight of patients were positively associated with the two responses where as visiting times were negatively associated with responses variables.

Recommendations

According to the results of this study the predictive factors of hypertensive and diabetes patients are more of behavioural and clinical variables, so health organizations or health workers should give awareness for such patients to modify their behavioural characteristics such as giving up smoking and attend their medication adherence properly according to the schedule given by health workers. Since hypertension and diabetes are among chronic diseases, individuals must be advisable to check up hypertension and fastingstatus of themselves regularly or in every situation especially older age and weighted patients.

Abbreviations

SBP=Systolic Blood pressure, DBP = diastolic blood pressure, AIC= Akakai information criterion,

BIC= Bayesian information criterion. LMM = Linear Mixed effect Model, SAS= Statistical Analysis System, OGTT = oral glucose tolerance test,

Declarations

Ethical approval and consent to participate*:* Informed consent form was not obtained from participants as the data was secondary. However, to get such secondary data, ethical clearance certificate had been obtained from Ethical committee of Bahir Dar University, Ethiopia with Ref RCS/1412/2006. We can attach the ethical clearances certificate up on request.

Consent for publication: *This manuscript has not been published elsewhere and is not under consideration by another journal. Both authors have approved for final manuscript and agreed to submit for publication with the given order of authors.*

Availability of data and materials: The secondary data used for current investigation is available with the corresponding author. The data available with corresponding author will not be made available publically since at the time the data were collected; informed consent form was not obtained from participants for publication of the dataset.

Competing interests: No conflict of interest between an author and institutions.

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Authors' contributions: *AS participated in collecting data, the design and data analysis, and GD critically read the manuscript for the betterment of the manuscript and approved for its submission.*

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References

1. Ginter, E. and V. Simko, *Global prevalence and future of diabetes mellitus*, in *Diabetes*. 2013, Springer. p. 35-41.
2. Gress, T.W., et al., *Hypertension and antihypertensive therapy as risk factors for type 2 diabetes mellitus.* New England Journal of Medicine, 2000. **342**(13): p. 905-912.
3. Gress, T.W., et al., *Hypertension and Antihypertensive Therapy as Risk Factors for Type 2 Diabetes Mellitus.*
4. Hansson, L., et al., *Effect of angiotensin-converting-enzyme inhibition compared with conventional therapy on cardiovascular morbidity and mortality in hypertension: the Captopril Prevention Project (CAPPP) randomised trial.* The Lancet, 1999. **353**(9153): p. 611-616.
5. Verdecchia, P., et al., *Adverse prognostic significance of new diabetes in treated hypertensive subjects.* Hypertension, 2004. **43**(5): p. 963-969.
6. Zhong, N.-s., et al., *Chinese guidelines for diagnosis and treatment of influenza (2011).* Journal of thoracic disease, 2011. **3**(4): p. 274.

7. Sowers, J.R., *Insulin resistance and hypertension*, 2004, Am Physiological Soc.
8. Abramson, J.L., W.S. Weintraub, and V. Vaccarino, *Association between pulse pressure and C-reactive protein among apparently healthy US adults.* Hypertension, 2002. **39**(2): p. 197-202.
9. Fieuws, S. and G. Verbeke, *Joint modelling of multivariate longitudinal profiles: pitfalls of the random-effects approach.* Statistics in medicine, 2004. **23**(20): p. 3093-3104.
10. Lala, P. and C. Chakraborty, *Factors Regulating Trophoblast Migration and Invasiveness: Possible Derangements Contributing to Pre-eclampsia and Fetal Injury1.* Placenta, 2003. **24**(6): p. 575-587.
11. Fitzmaurice, G., et al., *Longitudinal data analysis*. 2008: CRC Press.
12. Negash, Y., et al., *Joint modeling of longitudinal systolic and diastolic blood pressure measurements of hypertensive patients receiving treatment.* Electronic Journal of Applied Statistical Analysis, 2016. **9**(2): p. 308-325.
13. Davey, D.A. and I. MacGillivray, *The classification and definition of the hypertensive disorders of pregnancy.* American journal of obstetrics and gynecology, 1988. **158**(4): p. 892-898.
14. Gebregziabher, G., et al., *Economic analysis of factors influencing adoption of motor pumps in Ethiopia.* Journal of Development and Agricultural Economics, 2014. **6**(12): p. 490-500.
15. Control, C.f.D. and Prevention, *Increasing prevalence of diagnosed diabetes--United States and Puerto Rico, 1995-2010.* MMWR. Morbidity and mortality weekly report, 2012. **61**(45): p. 918.
16. Ong, K.L., et al., *Prevalence, treatment, and control of diagnosed diabetes in the US National Health and Nutrition Examination Survey 1999–2004.* Annals of epidemiology, 2008. **18**(3): p. 222-229.
17. MOLENBERGHS, G.V.G., *Longitudinal and incomplete clinical studies.* Metron, 2005. **63**(2): p. 143-176.
18. Vangeneugden, T., et al., *Applying concepts of generalizability theory on clinical trial data to investigate sources of variation and their impact on reliability.* Biometrics, 2005. **61**(1): p. 295-304.
19. Molenberghs, G., G. Verbeke, and C.G. Demétrio, *An extended random-effects approach to modeling repeated, overdispersed count data.* Lifetime data analysis, 2007. **13**(4): p. 513-531.
20. Campbell, N.R., et al., *Hypertension in people with type 2 diabetes: Update on pharmacologic management.* Canadian Family Physician, 2011. **57**(9): p. 997-1002.
21. Fieuws, S. and G. Verbeke, *Pairwise fitting of mixed models for the joint modeling of multivariate longitudinal profiles.* Biometrics, 2006. **62**(2): p. 424-431.
22. Guo, X. and B.P. Carlin, *Separate and joint modeling of longitudinal and event time data using standard computer packages.* The American Statistician, 2004. **58**(1): p. 16-24.

Tables

Table1: Baseline Demographic and clinical characteristics of hypertension and diabetes patients (n=748)

Characteristics	Average	Category	Frequency (n)	Percent (%)
Age in years	57 years			
Weight in kg	64 kg			
Height in meters	1.5m			
Baseline high blood pressure	146/105			
Sex		Female Male	362 386	48.4 51.6
Education level		illiterate primary Secondary and above	125 368 255	16.7 49.2 34.1
Residence		Rural Urban	225 523	30.1 69.9
Marital Status		Living with partner Living without partner	512 236	68.4 31.6
Education		Illiterate Primary Secondary and above	58 37 19	39.19 25 12.84
Smoking		No Yes	145 603	19.4 80.6
Chewing		No Yes	533 215	71.3 28.7
Alcohol		No Yes	421 327	56.3 43.7
Physical exercise		Never Rarely frequently	252 296 200	33.7 39.6 26.7
Consumption of meat		Never Rarely frequently	55 335 358	7.4 44.8 47.9
Consumption of vegetation		Never Rarely frequently	35 435 278	4.7 58.2 37.2
Family disease history (Diabetes or hypertensive)		No Yes	245 503	32.8 67.2

Table2: Parameter estimates and corresponding standard errors for joint marginal data analysis of hypertension and type2 diabetes with unstructured working covariance

Parameter	Hypertension			Type2 diabetes		
	Effect	Std. deviation	P-Value	Effect	Std. deviation	P-Value
Intercept	134.82/91.4	1.66	<.001	121	6.69	0.33
Age	0.18	0.16	0.04*	0.65	0.81	0.02*
Weight	0.52	0.15	<0.01*	0.71	0.38	<.01*
Physical exercise (Ref.= frequently)						
Never	6.85	2.69	0.23	27.33	2.80	0.75
rarely	2.23	0.23	0.14	5.32	1.52	0.15
Sex(Ref.=Male)						
Female	-1.97	3.47	0.01*	- 4.36	2.34	0.02*
Residence(Ref.=Urban)						
Rural	-1.09	2.4230	0.04*	-1.79	2.50	<0.01*
Marital Status(ref.=Single)						
Divorce	-14.51	7.95	0.08	-8.67	4.76	0.02
Married	-15.07	5.01	0.01	-9.90	3.85	<0.01
Smoking(Ref.=Yes)						
No	-0.65	1.61	0.03*	-1.39	6.26	0.04*
Chewing Chat(Ref.=Yes)						
No	-3.93	2.91	0.31	-1.65	3.73	0.96
Drinking alcohol(Ref.=Yes)						
No	-3.98	2.54	0.02*	-5.75	2.17	0.03*
Level of Education (Ref.=Tertiary)						
Illiterate	6.62	4.60	0.24	-9.42	2.29	0.72
Primary	5.71	4.34	0.28	13.27	2.14	0.59
Secondary	4.13	5.89	0.48	-5.06	2.08	0.85
Visiting time	-0.08	0.11	0.041*	-0.38	0.18	0.03*
Visiting time *sex(Ref.=Male)						
Female	-1.97	3.47	<0.01*	0.36	1.34	0.01*
Age* sex(Ref.=Male)						
Female	-1.27	4.47	0.01*	1.34	1.24	0.01*
Visiting time *Residence area(Ref.=Urban)						
Rural	-0.27	3.47	<0.01*	-0..26	1.34	0.02*

Table3: Parameter estimates and corresponding standard errors for conditional independence random intercept model with Hypertension and type2 diabetes data

Parameter	Hypertension			Type2 diabetes		
	effect	Std. deviation	P-Value	effect	Std. deviation	P-Value
Intercept	135/92	1.66	<.001	125.95	6.69	0.33
Age	0.18	0.16	0.04*	0.65	0.81	0.02*
Weight	0.52	0.15	<0.01*	0.71	0.38	<.01*
Physical exercise (Ref.= frequently)						
Never	6.85	2.69	0.023*	27.33	2.80	0.75
rarely	2.23	0.23	0.014*	5.32	1.52	0.15
Sex(Ref.=Male)						
Female	-1.97	3.47	0.010*	- 4.36	2.34	0.02*
Residence(Ref.=Urban)						
Rural	-1.09	2.4230	0.064	-1.79	2.50	<0.051
Family disease history for hypertension or diabetes(Ref.=yes)						
No	-4.25	1.45	0.023*	-2.62	1.52	0.020*
Marital Status (ref.= living without partner)						
Living with partner	-14.51	7.95	0.08	-8.67	4.76	0.02
Smoking(Ref.=yes)						
No	-0.65	1.61	0.03*	-1.39	6.26	0.04*
Chewing Chat(Ref.=yes)						
No	-3.93	2.91	0.31	-1.65	3.73	0.96
Drinking alcohol(Ref.=yes)						
No	-3.98	2.54	0.02*	-5.75	2.17	0.03*
Level of Education (Ref.=Tertiary)						
Illiterate	6.62	4.60	0.24	-9.42	2.29	0.72
Primary	5.71	4.34	0.28	13.27	2.14	0.59
Secondary	4.13	5.89	0.48	-5.06	2.08	0.85
Visiting time	-0.08	0.11	0.041*	-0.38	0.18	0.03*
Visiting time *sex(Ref.=Male)						
Female	-1.97	3.47	<0.01*	0.36	1.34	0.01*
Age* sex(Ref.=Male)						
Female	-1.27	4.47	0.01*	1.34	1.24	0.01*
Visiting time *Residence area(Ref.=Urban)						
Rural	-0.27	3.47	<0.01*	-0..26	1.34	0.02*

*stands for statistically significance

Table4: Parameter estimates for joint model of type2 diabetes data using linear predictor for hypertension.

Parameter	Effect	Std. deviation	95 % CI		P-Value
Intercept	126.95	6.69	-2.54	9.87	0.33
Age	0.65	0.81	0.03	0.98	0.02*
Weight	0.71	0.38	0.04	0.99	<0.01*
Hypertension	0.67	0.52	0.03	0.95	<0.01*
Visiting time	-0.38	0.18	-3.45	-0.54	0.03*
Physical exercise (Ref.= frequently)					
Never	2.33	0.80	0.87	4.15	< 0.01*
rarely	1.32	0.52	0.98	3.83	0.03*
Sex(Ref.=Male)					
Female	- 2.36	2.34	-4.43	- 0.65	0.02*
Residence(Ref.=Urban)					
Rural	-1.79	2.50	-3.98	-0.87	< 0.01*
Family disease history for hypertension or diabetes (Ref.=yes)					
No	-2.34	0.56	-4.45	-0.04	<0.01*
Marital Status (ref.= living without partner)					
Living with partner	-2.90	3.85	-4.23	- 0.75	<0.01*
Smoking(Ref.=Yes)					
No	-1.39	6.26	-3.24	-0.45	0.04*
Chewing Chat(Ref.=Yes)					
No	-1.65	3.73	-3.56	-0.45	0.03*
Drinking alcohol(Ref.=Yes)					
No	-3.75	2.17	-6.25	-0.53	0.03*
Level of Education (Ref.=Tertiary)					
Illiterate	9.42	2.29	-0.92	12.43	0.72
Primary	3.27	2.14	-1.76	5.34	0.59
Secondary	1.06	2.08	-2.32	3.42	0.85
Visiting time *sex(Ref.=Male)					
Female	-0.36	1.34	-2.01	-0.02	0.01*
Age* sex(Ref.=Male)					
Female	-1.34	1.24	-4.43	-0.54	0.01*
Visiting time *Residence area(Ref.=Urban)					
Rural	-1..26	1.34	-4.24	-0.45	0.02*

Comparing female patients with males, the amount of fasting glucose concentration in the blood of female patients was smaller than male patients keeping the other variables constant.

Figures

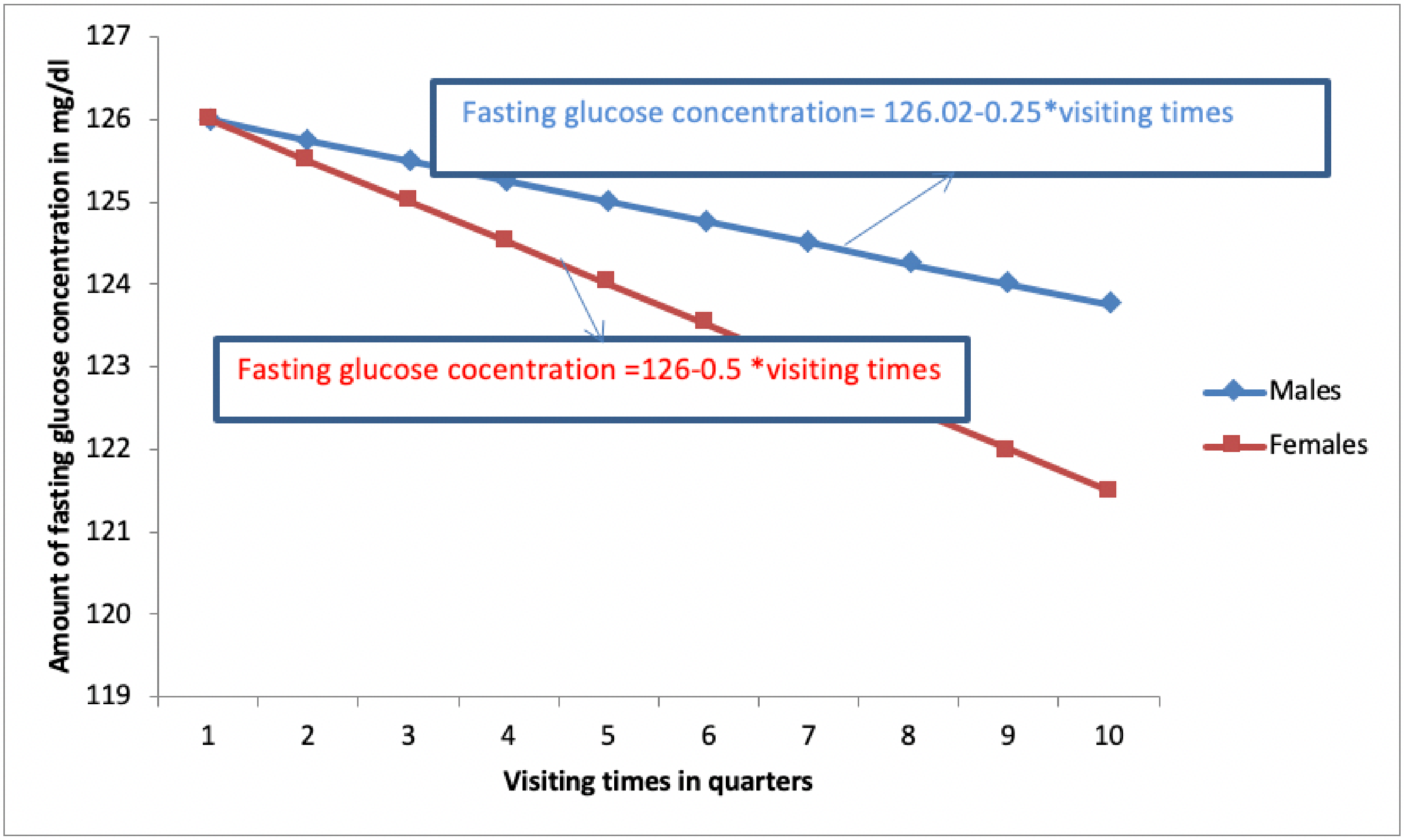

Figure 1

The plot of interaction effect between sex and visiting times of patients

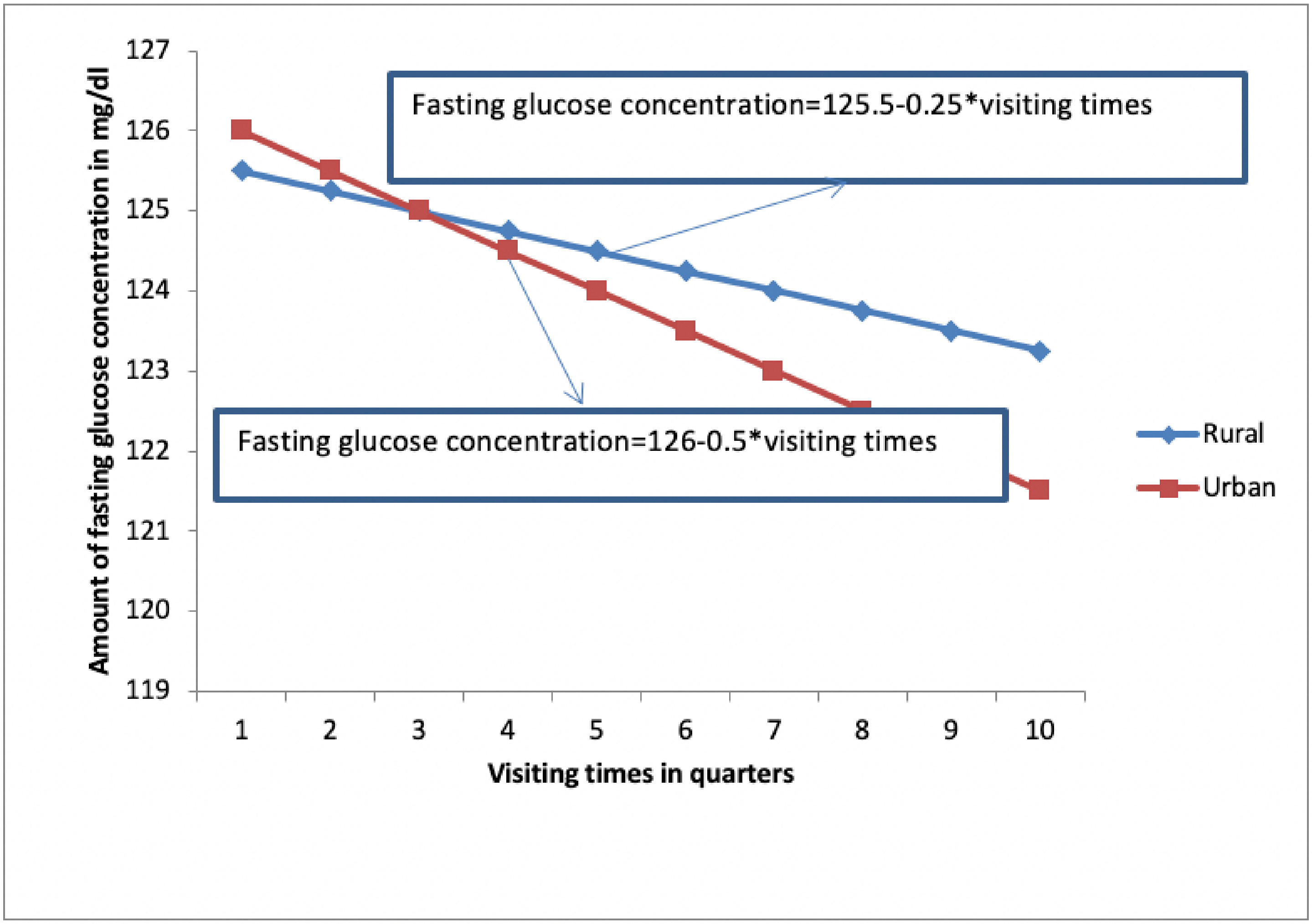

Figure 2

The plot of interaction effect between residence area and visiting times

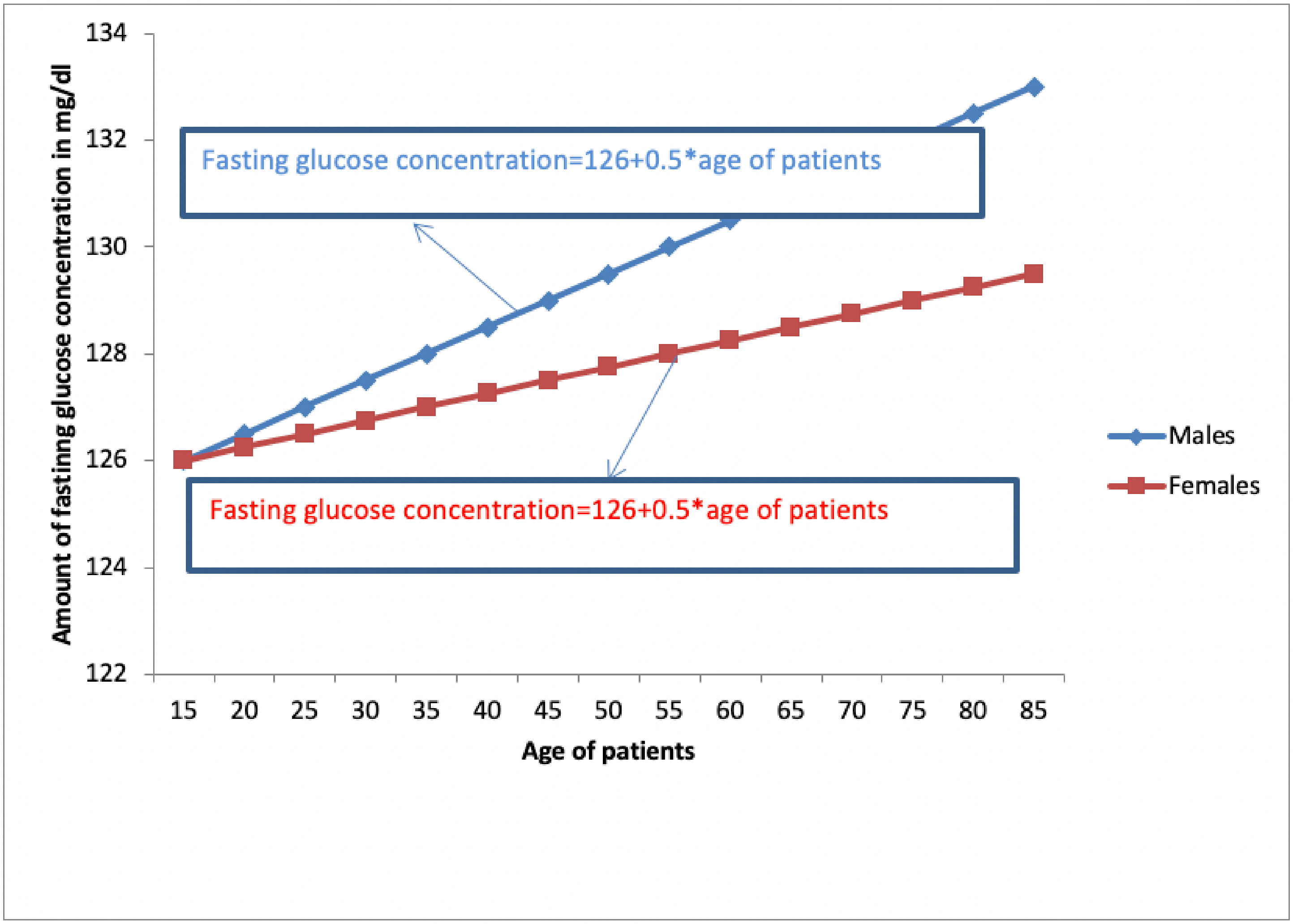

Figure 3

The plot of interaction effect between sex and age of patients