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Original Article

Factors affecting blood sugar changes in diabetic patients using a three-level model in analysis of longitudinal data

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Abstract

Background: Diabetes, a currently threatening disease, has severe consequences for individuals' health conditions. The present study aimed to investigate the factors affecting the changes in the longitudinal outcome of blood sugar using a three-level analysis with the presence of missing data in diabetic patients.

Methods: A total of 526 diabetic patients were followed longitudinally selected from the annual data collected from the rural population monitored by Tonekabon health centers in the North of Iran during 2018-2019 from the Iranian Integrated Health System (SIB) database. In analyzing this longitudinal data, the three-level model (level 1: observation (time), level 2: subject, level 3: health center) was carried out with multiple imputations of possible missing values in longitudinal data.

Results: Results of fitting the three-level model indicated that every unit of change in the body mass index (BMI) significantly increased the fasting blood sugar by an average of 0.5 mg/dl (p=0.024). The impact of level 1 (observations) was insignificant in the three-level model. Still, the random effect of level 3 (healthcare centers) showed a highly significant measure for health centers (14.62, p<0.001).

Conclusion: The BMI reduction, the healthcare centers' socioeconomic status, and the health services provided have potential effects in controlling diabetes.

Keywords: Blood sugar change, Diabetic patients, Body mass index, Health care centers, Three-level model, Missing data imputation, Longitudinal data.

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Diabetes has become one of the most prevalent noncontagious chronic illnesses in developing and developed countries over recent years. Because of its substantial financial burden and adverse health consequences, diabetes has become one of the world's most significant public health challenges in the 21st century (1). The epidemic dynamic of diabetes is accelerating and causing public health consequences like stroke, heart attack, amputation, and kidney disorders (2-4). This disease, more prevalent among adults in prosperous countries, has now spread to children and developing countries (5). Among those suffering from diabetes, some are unaware of their disease. For instance, around 5.2 million out of the 18.2 million diabetic patients in the USA were unaware of their condition in 2003 (3).

Diabetes is the fourth most prevalent reason for physician visits and the fifth dominant cause of mortality (6). Obesity and a sedentary lifestyle also increase the rate of this disease's prevalence (7). Research has shown that diabetes imposes an extremely high cost on families and the medical systems. Accordingly, the worldwide costs of diabetes were estimated at $132 billion in 2002, out of which $92 billion was spent on direct medical care costs and $40 billion on indirect costs (3). The latest statistics from the World Health Organization suggest that diabetes is growing fast in Asian countries. For instance, its prevalence has reached 3-5% in Iran (8).

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Moreover, around 1717 million people across the world had diabetes in 2000, which is estimated to grow to 4.4% in 2030 and 380 million people by 2025 (9-11). One of the follow-up measures for diabetic patients is a periodic fasting blood sugar (FBS) check which must be kept under 130 mg/dl. According to the Iranian Ministry of Health instructions, this measure must be taken at three-month intervals at medical care centers (11).

This means that each patient must refer to the respective healthcare center every season to check their blood sugar, BMI, blood pressure, and diabetes-related complications. Thus, this measure is recorded four times a year for each person. The repeated measurements associated with each person over various periods can be considered as a cluster. In other words, longitudinal data are a specific form of multilevel data since the measurement iteration (over specific intervals) is nested in subjects. The critical and characterizing features of longitudinal data are their correlation in repeated measurements over particular periods and their hierarchical structure at various levels (12, 13).

It provides a more accurate examination of the relationship between the studied outcome and the potential factors affecting it by accounting for the correlation structure between repeated measures over time within the subjects (14). Some studies incorporated a cluster structure and repeated measurements in which the assessments are related to the individual at the first level. The healthcare/medical centers are considered at the second, and other cluster structures (such as the comparison between counties) are taken into account at the third level. Models with various grades are used for analysis depending on the number of clustering levels (15). A hierarchical structure in data is the main reason behind the use of multilevel models.

Several studies assessed the relation of BMI with FBS. For example, a proper nutritional education on BMI reduction, the changes in FBS has been documented (16-18) However, they did not analyze with proper model with the longitudinal data to take into account the correlation structure of repeated measurement of FBS. The present study hypothesized that the role of patients in controlling their weight and, as a result, BMI positively impacts their blood sugar. This means that increasing awareness and self-care in patients (proper diet and regular exercise) is expected to reduce the blood sugar in the participants.

However, other variables, such as the role of healthcare providers in providing educational services and medical care, may also influence this relationship at a higher level, i.e., at the level of healthcare centers. This means that the quality of the services and training provided to patients by the healthcare providers at healthcare centers may leave positive or negative effects on the positive relationship between the decline in BMI and blood sugar (FBS, HbA1c) in diabetic patients. Multilevel analysis is imperative to measure the amount and intensity of the impact of this higher-level variable on the relationship between the two lower-level variables.

In this regard, few studies have considered a hierarchical structure of data and their internal correlation and missing data imputation in statistical analysis. Therefore, there is a paucity of data on Iranian diabetic patients. Another feature of longitudinal data is the presence of missing values in the follow-up of patients' measurements. Thus, the lack of appropriate imputation results in bias in the estimates and lower power of statistical tests. Therefore, we aimed to determine the influencing factors on blood sugar in diabetic patients using a three-level model with multiple imputations to handle missing data.

Methods

Study design and subjects: The present study is a longitudinal historical cohort study of 526 diabetic patients during two years of follow-ups in 2018-2019. In monitoring FBS, care is currently provided to diabetic patients in rural health community centers (healthcare houses) in Tonekabon county, the North of Iran. These health centers record the FBS of diabetic patients in the Integrated Health System (SIB) seasonally per year based on the instructions of the Iranian Ministry of Health. At present, the SIB system was designed and implemented to record and provide and update Iranian electronic record of health data and medical information.

The inclusion criteria were aging over 30 years, suffering from type 1 or 2 diabetes, having four annual FBS records in the SIB data-based system, and the presence of related data in the worksheet of the corresponding form in the Iranian recorded system. Suffering from gestational diabetes or diabetes-related serious consequences such as renal failure, cancer, and blindness were considered the exclusion criteria since their records were not available in the primary healthcare delivery SIB system. Typ1 diabetes is an autoimmune disease in which the affected person has insulin deficiency and typ2 diabetes is inability to use insulin properly due to insufficient insulin production and resistance of cells to the insulin they make and diabetes diagnosis was based on FBS over 126 (mg/dl) or the use of a hypoglycemic drug.

The study protocol was approved by the Institutional Board of Ethics Committee of Babol University of Medical Sciences, Iran (ethical code: IR. MUBABOL. REC. 110)

Sampling method: This longitudinal study recruited diabetic patients in various healthcare centers in the rural population of Tonekabon using two stage cluster sampling of 15 health centers, 3 health house from each center, and 12 patients from each health house. The allocated sample size of 526 is able to detect an effect size of 0.28 at the 95% confidence level and statistical power of 80%, with an internal correlation of ρ=90%, according to a similar study (19). The diabetic patients older than 30 were selected based on the inclusion criteria among the patients under the coverage of rural healthcare centers. Three healthcare houses were randomly chosen from every 15 rural centers through cluster sampling. Then, a minimum of 12 patients meeting the inclusion and exclusion criteria were randomly selected from each healthcare house, which totally amounted to 526 patients.

Data collection, variables, and tools: We used the SIB system database that routinely recorded the repeat measures of FBS and other measures four times each year. FBS was measured by Calorimeter method using Biomed kits and hemoglobin A1C with direct enzymatic method using Dyazim kits. After the patient entered the health center, the blood pressure was measured with a digital sphygmomanometer for a few minutes while sitting and resting. The data collection tool was a checklist containing information such as age, gender, diastolic blood pressure, systolic blood pressure, FBS, hemoglobin A1C, smoking, type of diabetes, family history of diabetes, history of hypertension, and body mass index (BMI), which is calculated by dividing the weight in kg by the square of the height in m^2. The demographic and clinical information of the patients at baseline were recorded in a predesigned checklist, and repeated measurements of fasting blood sugar were recorded every three months in the checklist.

Data analysis: In the statistical analysis phase, we used the two- level and three-level model. We assumed several patients with a random intercept and the presence of predictor variables. According to the hierarchical structure of the data, the first level is the observations of each person. The second level considers each individual, and the third level takes each healthcare center into account. Patients' characteristic was considered a fixed effect (see Appendix A for model specification). The goal of fitting this model is to investigate whether gender, age, smoking, genetic history of diabetes and healthcare services (the effect of the healthcare house) can have a significant relationship with the changes in blood sugar. The present study used STATA V.2.14 software to report the descriptive statistics, to fit the three-level model, and R V.2.1.4 for missing data imputation. A statistical significance level of 0.05 was considered for all two-sided tests.

Missing data imputation: Since a number of patients visited the healthcare centers (healthcare houses) over the follow-up (four times a year), might have needed to collect more data concerning their health status. The presence of missing data is inevitable in longitudinal data. Thus, analysis would be face serious threats such as data imbalance, missing information, reduced power, and biased estimation (17). In fact, the results lead to incorrect conclusions without a proper missing data imputed. Therefore, there was a need for missing data imputation or replacement. We used the Mice (Multivariate Imputation by Chained Equation) package in R software to assign missing data on continuous variables such as BMI and FBS. This imputation can be carried out through various techniques, among which the present study used the Fully Conditional Specification (FCS) (20).

The imputation algorithm replaced the missing data, and then the three-level model analysis was performed on data without any missing value. The FCS techniques used for multiple imputations of missing data are more flexible since they consider different conditions for every variable of the conditional model. Therefore, they are more suitable for cases where there are large numbers of variables (21).

Results

Missing data report: There were missing covariates and longitudinal outcome measurements across the study samples. We handled this matter using the MICE imputation methods using the FCS technique. The missing percentages of covariates are presented in table 1. These measures for the FBS longitudinal outcome at time 1 to time 4 were 8.75, 11.36, 9.33, and 9.35, respectively. **Demographic and clinical characteristics:** A total of 526 diabetic patients took part in the analysis. The mean and standard deviation of patients' age was 62.8 ±11.4, with the males representing 352 (66.9%) of the total sample. About 71% of the patients had a genetic history of diabetes, 54% had a hypertension history. Moreover, 97.3% of the patients had type 2 diabetes.

Other information about demographic variables in the form of frequency and percentage for qualitative variables and mean and standard deviation for quantitative variables are presented in table 2.

Table1. Missing percentage of covariates and longitudinal outcome

Variables	%
Sex	2.04
Age	2.04
Type of DM	2.04
Hypertension history	2.04
Smoking	2.04
Family history of diabetes	7.42
BMI	8.57
HbA1C	30.17
FBS	8.75
SBP	8.38

DM: Diabetes mellitus, BMI: body mass index, HbA1C: hemoglobin A1C, FBS: Fasting blood sugar, SBP: Systolic blood pressure

Table 2. Demographic and clinical features in diabetic patients at baseline

Characteristics Categorical variables Sex	n(%)
Male	174(33.1)
Female	352(66.9)
Smoking	
Yes	51(10.2)
No,	475(89.8)
Family history of diabetes	
Yes	144(29.0)
No	352(71.0)
Hypertension history	
Yes	286(54.4)
No	240(45.6)
Type of DM	
Type 1	14(2.7)
Type 2	512(97.3)
Quantitative variables	Mean±SD
Age(years)	62.8±11.40
BMI(kg/m^2)	28.94±4.55
FBS (mg/dl)	153.31±45.25
HbA1C	7.05±1.14
SBP (mm Hg)	12.25±0.91
DBP (mm Hg)	7.77±0.64

DM: Diabetes mellitus, BMI: Body mass index, FBS: Fating blood sugar, HBA1C: Hemoglobin A1C, SBP: Systolic blood pressure, DBP: Diastolic blood pressure.

Fitting three-level model with MICE imputation methods for missing data: Table 3 indicates that one-unit increase in BMI enhances the value of FBS by 0.50 units. The impact of level 1 (observation) was insignificant in the three-level model, and its regression coefficient was almost negligible (p=0.99). The impact of level 3 (healthcare centers) was 14.6, statistically significant, which shows the heterogeneous variance of FBS between health centers (p<0.001). In addition, the significant effects of diabetes (p<0.001), family history of diabetes (p<0.001), and SBP (p=0.002) variables were observed in increasing the FBS levels.

Table 3. Results of fitting the three-level model using MICE imputation method for missing data

Variables	$\hat{\beta}$ (95%CI)	SE ($\hat{\beta}$)	p
Sex (Male vs Female)	-0.89 (-5.81,4.02)	2.51	0.722
BMI, (kg/m^2)	0.50 (0.07,0.93)	0.22	0.024
Age, (year)	0.14 (-0.05,0.33)	0.10	0.157
Smoking (Yes vs No)	0.40 (-6.91,7,71)	3.72	0.915
Type of diabetes (type 1 vs type2)	27.29 (11.99,42.59)	7.81	<0.001
Hypertension history(Yes vs No)	2.68 (-2.22,7.58)	2.50	0.283
Family history of diabetes (Yes vs No)	-13.82 (-18.37, -9.27)	2.32	<0.001
SBP (mm Hg)	4.11 (1.57,6.65)	1.29	0.002
Intercept	-21.16 (-84.64,42.32)	32.36	0.513
Level 1(time)	-	<0.001	<0.99
σ^2 Level 2	40.37 (38.84,41.97)	0.79	<0.001
σ^2 Level 3	14.62 (11.47,18.62)	1.80	<0.001

BMI: Body mass index, SBP: Systolic blood pressure, σ^2: Variance

Discussion

Our research explored the positive effect of BMI on changes in FBS after adjusting potential confounding factors in our three-level model. The remarkable findings of the current study can be of great help to future researchers whose work investigates the impact of BMI and seeks to control the other confounding variables. Our findings show a positive association between BMI and change in blood sugar after adjusting for potential confounders in the three-level model which is consistent with many other studies (16-18). This result highlights the importance of providing interventional educational programs for weight reduction and hypoglycemia treatment to control diabetes. In addition, based on current research findings, in the random effect model coefficient of the three-level model, a significant heterogeneous variance was observed between the health centers in explanation of the variation of blood sugar. This heterogeneity indicates the variation difference due to health centers providing primary and secondary preventive care for diabetic control. This variation can be either explained by the differences in the socio-economic and educational levels of the surrounding environment or the various experiences of health caregivers in providing preventive care for diabetic patients. In addition, these variations might be due to other unknown social and cultural factors and individual factors that were not measured directly in the current study. Therefore, it would be better to use the three-level model and not eliminate or attenuate the effect of centers from the main results.

Other results of the three-level model fitness in the present study indicated that the diabetes type, genetic background, and systolic hypertension were the factors affecting the changes in blood sugar in the diabetic patient population. Therefore, the healthcare centers or the neighborhood where the patients lived left significant impacts on their fasting blood sugar. A similar finding had been observed in terms of availability of health care, socioeconomic status, the environment of residence, and other unknown factors related to community-level associated with changing blood sugar and incidence of type 2 diabetes (21, 22). Since it would be difficult to identify some unknown factors, the present multi-level model accounted for the influence of healthcare centers as one of the factors of one's place of residence to locate and test its influence. In general, the result of the present study is in line with previous studies (23-27). Thus, it would be better to pay closer attention to the unknown social and personal factors when determining the factors affecting the blood sugar of diabetic patients. Therefore, multi-level models can be used to identify and control these factors. However, our findings did not show a significant trend of changes in blood sugar over the follow-up time. This may imply that the patients and the health caregivers provided adequate care to control diabetes over the time examined.

The present study has several advantages. The three-level model we used considers the correlation between each individual's observations to estimate the regression coefficients and their proper SE and thus yield a valid statistical test of individual characteristics as determinants of FBS. In the current study, since the FBS longitudinal response and time are dependent variables that usually have missing values in longitudinal assessment, the missing value also needs to be handled. Also, there is more efficiency needed in the study outcomes in the longitudinal data structure. Several methods of missing imputation have been proposed (28). However, the performance of the multiple imputations by the FCS technique used in the present study yields an unbiased estimate of the effect measured (29). This method is more flexible when there are numerous variables with missing data. In fact, there is a specific conditional model for each variable separately to impute the relevant missing value. In particular, when the missing value occurs at a random pattern (MAR), this method results in an unbiased estimate of the desired effect (29). While most researchers omit the missing records in regression modeling, others impute its average value as observations over time.

The results should be generalized cautiously. The missing imputation in the present study required an assumption of missing at random (MAR) to generate objective estimations for missing values. However, the missing data may not have been accidental. In this case, the loss of data will depend on the conditions that occurred (30).

The findings show an increase in BMI elevates the blood sugar changes and the heterogeneous variance of coefficient due to health centers in the three-level model that implies the role of community-level factors and the difference in providing health care by various health centers in controlling diabetes.

Appendix A

The three-level model: The equation for level-1 model is

$$FBS_{ijk} = \beta_{0jk} + \beta_{1jk} Time_{ijk} + e_{ijk} e_{0jk} \sim N(0.\sigma_e^2)$$

Where FBS_{ijk} is the FBS at time I for patient j in healthcare center k ; β_{0jk} is the FBS for patient j in healthcare center k , that is, the expected outcome for patient j in healthcare center k when time point = 0; β_{1jk} is the change of FBS for patient j in healthcare center k; $Time_{ijk}$ is the patient level time predictor at time i for patient j in healthcare center k; and e_{ijk} is the residual associated with a patient's score at a specific time point, which is assumed to be normally distributed with a mean of 0 and variance of σ_e^2. The level-2 equations are

$$\beta_{0jk} = \alpha_{00k} + \alpha_{01k} X_{jK} + u_{0jk} u_{0jk} \sim N(0.\sigma_{u0}^2)$$

$$\beta_{1jk} = \alpha_{10k} + \alpha_{11k} X_{jK} + u_{1jk} u_{1jk} \sim N(0.\sigma_{u1}^2)$$

Level 3 model: where α_{00k} represents the mean of FBS for healthcare center k, and u_{0jk} is the variation in FBS among patients within-healthcare center. α_{10k} is the mean of change in FBS for healthcare center k and u_{1jk} is the variation in change of FBS among patient within-healthcare u_{0jk} and u_{1jk} are assumed to be in multivariate normal distribution, each with a mean of 0, and variance σ_{u0}^2 ,σ_{u1}^2, respectively. α_{11k} is indicates the mean increase in the response variable for every unit of change in the predictor variable of $\boldsymbol{X}_{jk}$. The level-3 equations are as follows

$$\alpha_{00k} = \delta_{000} + \nu_{00k} \nu_{00k} \sim N(0.\sigma_{v00}^2)$$

$$\alpha_{10k} = \delta_{100} + \nu_{10k} \nu_{10k} \sim N(0.\sigma_{v10}^2)$$

$$\alpha_{11k} = \delta_{100} + \nu_{10k} \nu_{11k} \sim N(0.\sigma_{v11}^2)$$

Where δ_{000} represents the mean FBS, and ν_{00k} is the variation in FBS across healthcare center. δ_{100} represents the mean change of FBS, and ν_{10k} is the variation in change of FBS across healthcare center. ν_{00k} and ν_{10k} are assumed to be in multivariate normal distribution, each with a mean of 0, and variance σ_{v00}^2 ,σ_{v10}^2 *and* other notation have the same interpretation (31). Thus, the combined model is:

$$FBS_{ijk} = \delta_{000} + \nu_{00k} + (\delta_{010} + \nu_{01k})X_{jK} + u_{0jk} + (\delta_{100} + \nu_{10k} + (\delta_{100} + \nu_{10k})X_{jK} + u_{1jk})\, Time_{ijk} + e_{ijk}$$

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Data availability statement: Data are available from the corresponding author for a reasonable request.

Patient consent for publication: All patients had given written consent prior to participation in the study.

Conflict of Interests: The authors declare that there are no conflicts of interest.

Authors' contribution: TR contributed to the conception of design, data collection, analysis, and writing of the first draft of the manuscript. KH contributed to the supervision of the study, design conception, analysis, and writing and revising of the manuscript. MH also contributed to the study design, analysis, and critical revision of the manuscript. BH contributed the design conception of the clinical aspect of the study. NRR and ZG also contributed to data collection, analysis, and interpretation of data and drafting of the manuscript.

References

1. Zimmet PZ, Magliano DJ, Herman WH, Shaw JE. Diabetes: a 21st century challenge. Lancet Diabetes Endocrinol 2014; 2: 56-64.
2. Norris SL, Nichols PJ, Caspersen CJ, et al. The effectiveness of disease and case management for people with diabetes: a systematic review. Am J Prev Med 2002; 22: 15-38.
3. Strine TW, Okoro CA, Chapman DP, et al. The impact of formal diabetes education on the preventive health practices and behaviors of persons with type 2 diabetes. Prev Med 2005; 41: 79-84.
4. Clement S. Diabetes self-management education. Diabetes Care 1995; 18: 1204-14.
5. Abazari P, Vanaki Z, Mohammadi E, Amini M. Inadequate investment on management of diabetes education. J Res Med Sci 2012; 17: 792-8.
6. Baghianimoghadam MH, Afkhami Ardekani M. The effect of educational intervention on quality of life of diabetic patients type 2, referee to diabetic research centre of Yazd. Intern Med Today 2008; 13: 21-8.
7. Karimy M, Eshrati B. The effect of health promotion model-based training on promoting students' physical activity. J Kermanshah Uni Med Sci 2012; 16: 192-200. (in Persian).
8. Shahrakivahed A, Haghighi M, Nrouei F, Heydari M. A study on the assessment of educational needs of diabetic patients. J Diabetes Nurs 2013; 1: 31-7.
9. EydiBaygi M, Mehrabizade M, Davoudi I, Ahmadi V, Dehghanizade Z. Comparison the quality of life in patients with diabetes type 2 and non-diabetic individuals. J ILAM Uni Med Sci 2014; 22: 55-62. (in Persian)
10. Ala M, TabatabaiMolazi A, Sanjari M, Mohajeri Tehrani M. The Role of nurses in the prevention and treatment of diabetic foot. Iran J Diabetes Lipid Diso 2011; 5: 472-80. (in Persian)
11. Taghdisi MH, Borhani M, Solhi M, Afkari M, Hosseini M. Effect of educational program based on PRECEDE model on quality of life in patients with typeII diabetes. J Gorgan Uni Med Sci 2011; 13: 29-36. (in Persian)
12. Zayeri F, Amini M, Moghimbeigi A, Soltanian AR, Kholdi N, Gholami-Fesharaki M. Application of Bayesian hierarchical model for detecting effective factors on growth failure of infants less than two years of age in a multicenter longitudinal study. Iran Red Crescent Med J 2016; 18: e36732.
13. Wang X, Armstrong M, Cairns B, Key T, Travis R. Shift work and chronic disease: the epidemiological evidence. Occup Med (Lond) 2011; 61: 78-89.
14. Kwok OM, Underhill AT, Berry JW, et al. Analyzing longitudinal data with multilevel models: an example with individuals living with lower extremity intra-articular fractures. Rehabil Psychol 2008; 53: 370-86.
15. Aitkin M, Anderson D, Hinde J. Statistical modelling of data on teaching styles. J R Stat Soc Ser A 1981; 144: 419-48.
16. Vittal B, Praveen G, Deepak P. A study of body mass index in healthy individuals and its relationship with Fasting blood sugar. J Clin Diag Res 2010; 4: 3421-4.
17. Prema G, Anitha R, Padmini O. Relation between Body Mass Index (BMI) and Fasting Blood Sugar (FBS). Int J Contem Med Res 2016: 3: 91-4.
18. Heydari GH, Moslemi S, Heydari Q, Kebriaei A. Effects of proper nutrition education on BMI reduction and changes on FBS, chol and TG rates of type 2 diabetic patients. J Med Sci 2006; 6: 374-7.

19. Reisi M, Mostafavi F, Javadzade H, et al. Impact of health literacy, self-efficacy, and outcome expectations on adherence to self-care behaviors in Iranians with type 2 diabetes. Oman Med J 2016; 31: 52-9.
20. De Silva AP, Moreno-Betancur M, De Livera AM, Lee KJ, Simpson JA. A comparison of multiple imputation methods for handling missing values in longitudinal data in the presence of a time-varying covariate with a non-linear association with time: a simulation study. BMC Med Res Methodol 2017; 17: 1-11.
21. Consolazio D, Koster A, Sarti S, et al. Neighbourhood property value and type 2 diabetes mellitus in the Maastricht study: A multilevel study. PLoS One 2020; 15: e0234324.
22. Carlin J. Multiple imputation: a perspective and historical overview. Handbook of missing data. 1st (ed). New York 2015; pp: 239-61.
23. Talukder A, Hossain M. Prevalence of diabetes mellitus and its associated factors in Bangladesh: application of two-level logistic regression model. Sci Rep 2020; 10: 1-7.
24. Aheto JMK, Dagne GA. Multilevel modeling, prevalence, and predictors of hypertension in Ghana: Evidence from Wave 2 of the World Health Organization's Study on global AGEing and adult health. Health Sci Rep 2021; 4: e453.
25. Khashayar P, Kasaeian A, Heshmat R, et al. Childhood overweight and obesity and associated factors in iranian children and adolescents: a multilevel analysis; the CASPIAN-IV study. Front Pediatr 2018; 6: 393.
26. Nguyen NT, Nguyen XM, Lane J, Wang P. Relationship between obesity and diabetes in a US adult population: findings from the National Health and Nutrition Examination Survey, 1999-2006. Obes Surg 2011; 21: 351-5.
27. Banegas JR, López-García E, Graciani A, et al. Relationship between obesity, hypertension and diabetes, and health-related quality of life among the elderly. E Eur J Cardiovasc Prev Rehabil 2007; 14: 456-62.
28. Mavridis D, White IR. Dealing with missing outcome data in meta-analysis. Res Synth Methods 2020; 11: 2-13.
29. Huque MH, Carlin JB, Simpson JA, Lee KJ. A comparison of multiple imputation methods for missing data in longitudinal studies. BMC Med Res Methodol 2018; 18: 1-16.
30. Rubin DB. Inference and missing data. Biometrika 1976; 63: 581-92.
31. Lee E, Hong S. Adequate sample sizes for a three-level growth model. Front Psychol 2021; 12: 685496.