The Chittagong Univ. J. Sci. 44(1): 51-62, 2022

Effect of Obesity on Developing Diabetes in Adult Population

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Manuscript Submitted on 07/10/2021, Revised manuscript received on 05/04/2022, and accepted on 05/06/2022.

Abstract

Diabetes is a kind of metabolic disease characterized by high blood glucose. High blood glucose occurs because of insufficient secretion of insulin by the pancreas or inability of body's cells to react properly to insulin or both. Problem with eyes, kidney failure, heart attacks, stroke and lower limb amputation are the possible long term effect of diabetes. An important indicator of glycemic control in diabetes is the level of Glycosylated hemoglobin (HbA1c). According to WHO an HbA1c of 6.5% is recommended as the cut point for diagnosing diabetes. This study focuses on the effect of obesity ($BMI \geq 30$) of the adults individuals on their HbA1c level based on a longitudinal data. The data for the study were collected from Health and Retirement Study (HRS) sponsored by the National Institute of Aging and conducted by the University of Michigan in USA. It is a nationwide cohort study for Americans over age 50 and their spouses. Profile analysis for longitudinal data is used in the study. Both classical and Bayesian approaches have been applied to carry out the study. The study shows that mean HbA1c is higher in all the time points for the individuals with obesity. Also the steeper trend line of mean HbA1c for individuals with obesity implies that, they are more likely to develop diabetes compared to other.

Keywords: *HbA1c, Body Mass Index(BMI), Bayesian approach.*

DOI: https://doi.org/10.3329/cujs.v44i1.64428

ডায়াবেটিস হল এক ধরনের বিপাকীয় রোগ যা রক্তে উচ্চমাত্রার গ্লুকোজ দ্বারা চিহ্নিত করা হয়। অগ্ন্যাশয় দ্বারা ইনসুলিনের অপর্যাপ্ত নিঃসরণ বা ইনসুলিনের প্রতি শরীরের কোষগুলোর সঠিকভাবে প্রতিক্রিয়া জানানোর অক্ষমতা বা উভয় কারণে রক্তে উচ্চমাত্রার গ্লুকোজ হয়ে থাকে। চোখের সমস্যা, কিডনি বিকল হওয়া, হার্ট অ্যাটাক, স্ট্রোক এবং নিম্নাঙ্গের অঙ্গচ্ছেদ ডায়াবেটিসের সম্ভাব্য দীর্ঘমেয়াদী প্রভাব। ডায়াবেটিসে গ্লাইসেমিক নিয়ন্ত্রণের একটি গুরুত্বপূর্ণ সূচক হল গ্লাইকোসাইলেটেড হিমোগ্লোবিনের (HbA1c) এর মাত্রা। WHO এর মতে ডায়াবেটিস নির্ণয়ের জন্য HbA1c ৬.৫% কে কাট পয়েন্ট হিসেবে সুপারিশ করা হয় । এ গবেষণায় একটি অনুদৈর্ঘ্য তথ্যের উপর ভিত্তি করে প্রাপ্ত বয়স্ক ব্যক্তিদের HbA1c স্তরে তাদের অতিশয় স্থূলতার ($BMI \geq 30$) প্রভাবের উপর দৃষ্টি নিবদ্ধ করা হয়েছে। গবেষণার তথ্য যুক্তরাষ্ট্রের ন্যাশনাল ইনস্টিটিউট অব এজিং -এর পৃষ্ঠপোষকতা এবং মিশিগান বিশ্ববিদ্যালয় কর্তৃক পরিচালিত হেলথ অ্যান্ড রিটাডারমেন্ট স্টাডি (HRS) থেকে সংগ্রহ করা হয়েছে। এটি ৫০ বছরের বেশি বয়সী আমেরিকানদের এবং তাদের পত্নীদের জন্য একটি দেশব্যাপী সমষ্টিগত গবেষণা। গবেষণাটিতে অনুদৈর্ঘ্য তথ্যের জন্য প্রোফাইল বিশ্লেষণ পদ্ধতি ব্যবহার করা হয়েছে এবং ক্লাসিক্যাল পদ্ধতির সাথে বেইজিয়ান পদ্ধতিরও প্রয়োগ করা হয়েছে। গবেষণায় দেখা গেছে যে, স্থূলতায় আক্রান্ত ব্যক্তিদের জন্য গড় গ্লাইকোসাইলেটেড হিমোগ্লোবিনের (HbA1c) এর মাত্রা সব সময়ই বেশি। এছাড়াও স্থূলতায় আক্রান্ত ব্যক্তিদের জন্য গড় গ্লাইকোসাইলেটেড হিমোগ্লোবিনের (HbA1c) এর স্টিপার ট্রেন্ড লাইন বোঝায় যে, অন্যদের তুলনায় তাদের ডাযাবেটিস হওয়ার সম্ভাবনা বেশি।

1. Introduction

Good glycemic control is essential in preventing diabetic complications. Glycosylated hemoglobin (HbA1c) is an important indicator of glycemic control in diabetes mellitus, based on which important diagnostic and therapeutic decisions are routinely made. Diabetes mellitus has assumed epidemic proportions worldwide, causing much morbidity and mortality on account of its various complications. The development of chronic vascular complications of diabetes such as retinopathy, nephropathy and cardiovascular disease is intimately linked to the level of glycemic control attained by the individual with diabetes [1].

Glycated hemoglobin (HbA1c) was first described by Rahbar et al. in 1969 [2]. Subsequent studies showed that the level of HbA1c correlated well with the glycemic control over a period of 2 to 3 months, leading to the gradual incorporation

of the test into clinical practice in the 1980s [3]. The level of glycosylated hemoglobin (HbA1c) provides a measure of the glycemic control of diabetes patients during the previous 2–3 months [4]. According to WHO an HbA1c of 6.5% is recommended as the cut point for diagnosing diabetes [5].

Body mass index (BMI) is a person's weight in kilograms divided by the square of height in meters. BMI is an inexpensive and easy screening method for weight category as obesity (30+), pre obesity (25.0-29.9), normal weight (18.5-24.9), and underweight (<18.5) according to World Health Organization.

BMI does not measure body fat directly, but BMI is moderately correlated with more direct measures of body fat [6]. Furthermore, BMI appears to be as strongly correlated with various metabolic and disease outcome as are these more direct measures of body fatness [7]. A healthy weight sets the stage for bones, muscles, brain, heart, and others to play their parts smoothly and efficiently for many years. Excess weight, especially obesity, diminishes almost every aspect of health, from reproductive and respiratory function to memory and mood.

In this study attempt was made to know the effect of the obesity on glycated hemoglobin (HbA1c) in adult population.

2. Data

Data for this study were obtained from Health and Retirement Study (HRS) via approval from the concerned authority. The HRS is sponsored by the National Institute of Aging and conducted by the University of Michigan and is a nationwide cohort study for Americans over age 50 and their spouses. Starting from 1992, for every two years time sampled individuals were followed. For the HbA1c measurements of individuals, 2006 Biomarker Data (HRS) [8], 2010 Biomarker Data (HRS) [9], and 2014 Biomarker Data (HRS) [10], were merged with randhrs

1992-2016 data file. HbA1c levels of the individuals were first taken in 2006 and then they were followed for the same in 2010 and 2014. As a result the data set is a longitudinal one.

3. Method

Profile analysis, which is a special case of the repeated-measures analysis by MANOVA (Box, 1950; see also Geisser and Greenhouse, 1958; Greenhouse and Geisser, 1959) [11, 12, 13] is used in our study. Profile analysis is used to compare different groups of subjects in terms of mean response over time. It is generally useful for balanced longitudinal designs and when there is a single categorical covariate (perhaps denoting different treatment or exposure groups), which is the situation in present study. Individuals' level of HbA1c is considered as response variable and body mass index (BMI) categorized as obesity, pre obesity, normal weight, and underweight is used as covariate in our study. Bayesian approach in profile analysis is also applied here through WinBUGS.

4. Results and Discussion

4.1 Classical Approach

Using complete cases the study was conducted over 3281 individuals. Where 1115 individuals were found having BMI 30 and above and considered in obesity class, 1295 individuals in pre obesity having BMI 25.0-29.9, 844 individuals in normal weight having BMI 18.5-24.9, and the rest 27 in underweight with BMI less than 18.5.

The mean HbA1c level over times based on classified body mass index (BMI) are shown in the following table.

Table 1. Mean HbA1c over times based on BMI of the respondents

		Measurement occasions		
Group	**Number**	**2006**	**2010**	**2014**
Obesity	1115	5.988	6.123	6.299
Pre Obesity	1295	5.737	5.817	5.947
Normal weight	844	5.565	5.647	5.727
Underweight	27	5.415	5.540	5.764

It is seen that mean HbA1c are highest over times for obesity followed by pre obesity and normal weight. Graphical presentation shows that

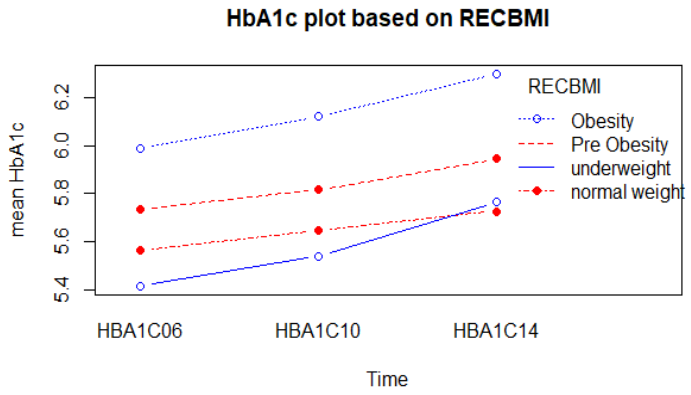

Figure 1. Mean HbA1c over times based on recoded BMI of the respondents

mean HbA1c level are higher for obesity and pre obesity compared to normal weight. Underweight has least HbA1c in 2006 and 2010 although it is somewhat higher than normal weight in 2014. Another thing is that, an increasing trend in mean HbA1c level is seen over times in all categories and it is steeper for obesity class. Increasing trend in mean HbA1c level implies that as people ages the probability of developing diabetes also increases and people with obesity are more likely to develop diabetes compared to other.

The results of the profile analysis model with HbA1c as response variable and recoded BMI (obesity, pre obesity, normal weight and underweight) as covariate are shown in the following table

Table 2. Results of profile analysis model with HbA1c as response variable and recoded BMI as covariate.

	DF	**F-value**	**p-value**
(Intercept)	1	194874.4	<.0001
RECBMI	3	66.92	<.0001
year.f	2	111.83	<.0001
RECBMI:year.f	6	2.62	0.0154

Above results shows significant effect of Recoded BMI (RECBMI) and year. f (time) on HbA1c level of the respondents. Their interaction is also significant.

REML estimates of the regression coefficients and standard errors are shown in the following table

Table 3. Estimated regression coefficients and standard error based on profile analysis model with HbA1c as response variable and recoded BMI as covariate.

	Estimate	**Std.Error**	**t-value**	**p-value**
(Intercept)	5.5651	0.0291	191.4147	0.0000
Obesity	0.4232	0.0385	10.9829	0.0000
Pre Obesity	0.1718	0.0374	4.5966	0.0000
underweight	-0.1499	0.1651	-0.9076	0.3641
year.f10	0.0818	0.0278	2.9449	0.0032
year.f14	0.1621	0.0308	5.2544	0.0000
Obesity:year.f10	0.0531	0.0368	1.4439	0.1488
Pre Obesity:year.f10	-0.0013	0.0357	-0.0368	0.9706
underweight:year.f10	0.0434	0.1577	0.2752	0.7832
Obesity:year.f14	0.1487	0.0409	3.6366	0.0003
Pre Obesity:year.f14	0.0484	0.0396	1.2212	0.2220
underweight:year.f14	0.1872	0.1752	1.0683	0.2854

Normal weight and year.f 06 (year 2006) are considered here as reference category. From the table we see that obesity and pre obesity have significantly higher HbA1c compared to normal weight. Significant positive effect for year.f10 (year 2010) and year.f14 (year 2014) compared to year.f06 (year 2006) implies that, there is an increasing trend in HbA1c level over times. Again interaction effect of obesity and year.f14 is also significant. Thus it can be concluded that as people ages they are likely to develop high HbA1c level and people with obesity are more likely to develop diabetes compared to other category.

4.2 Bayesian Approach

The Analysis is also performed by Bayesian approach using WinBUGS based on the BUGS CODE [14] (given in Appendix) with 50000 observations for the simulation, with 1000 starting values and a refresh of 100.

Table 4. Posterior Analysis of mean profile of HbA1c for recoded BMI

parameter	mean	sd	MC error	2.5 %	median	97.5 %
beta1	5.8280	0.0326	0.0002	5.7630	5.8280	5.8920
beta2	0.1553	0.0134	0.0001	0.1288	0.1553	0.1817
beta3	5.6260	0.0301	0.0003	5.5670	5.6260	5.6850
beta4	0.1048	0.0124	0.0001	0.0807	0.1048	0.1294
beta5	5.4840	0.0373	0.0003	5.4110	5.4840	5.5570
beta6	0.0812	0.0154	0.0001	0.0511	0.0812	0.1112
beta7	5.2300	0.2097	0.0018	4.8190	5.2300	5.6450
beta8	0.1737	0.0863	0.0008	0.0048	0.1735	0.3421
d13	0.2017	0.0444	0.0004	0.1148	0.2017	0.2889
d15	0.3440	0.0498	0.0004	0.2461	0.3442	0.4423
d17	0.5981	0.2121	0.0018	0.1797	0.5991	1.0120
d24	0.0504	0.0183	0.0001	0.0146	0.0505	0.0863
d26	0.0741	0.0205	0.0002	0.0339	0.0741	0.1141
d28	-0.0185	0.0873	0.0008	-0.1889	-0.0187	0.1530
d35	0.1423	0.0480	0.0004	0.0483	0.1421	0.2366
d37	0.3964	0.2117	0.0019	-0.0209	0.3960	0.8112
d46	0.0237	0.0198	0.0002	-0.0150	0.0237	0.0625
d48	-0.0689	0.0873	0.0008	-0.2401	-0.0688	0.1022
d57	0.2541	0.2125	0.0018	-0.1640	0.2540	0.6709
d68	-0.0926	0.0876	0.0008	-0.2636	-0.0927	0.0797

Table 4 shows that posterior mean of intercepts is 5.8280 for obesity, 5.6260 for pre obesity, 5.4840 for normal weight and 5.2300 for underweight. That is intercept is highest in obesity, followed by pre obesity, normal weight and underweight. Slopes of time also follow the same trend.

Bayes approach helps us in determining credible intervals of the estimators. We see that 95% credible intervals of d13 (0.1148, 0.2889), d15 (0.2461, 0.4423), d17 (0.1797, 1.0120), d35 (0.0483, 0.2366), d24 (0.0146, 0.0863), and d26 (0.0339, 0.1141) do not contain zero. That is they are significant. Therefore respondents with obesity have significantly higher HbA1c compared to pre obesity, normal weight and underweight. Respondents with pre obesity also have significantly higher HbA1c than normal weight. Slope coefficient of time for obesity is also significantly higher than pre obesity and normal weight. Comparing table 03 and table 04 it is seen that, in most of the cases standard errors of different estimators are smaller in Bayes method compared to their classical counterpart.

5. Conclusion

The above analysis, graphs, and posterior results of Bayesian methods depicts that, obesity plays a significant role on blood sugar level for adult population. People with obesity are more likely to develop high HbA1c compared to others. Thus standard weight should be maintained in order to lead a healthy and happy life.

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Appendix

BUGS CODE

```
model {
# prior distribution
beta1~dnorm(0.0, 0.001)
beta2~dnorm(0.0, 0.001)
beta3~dnorm(0.0, 0.001)
beta4~dnorm(0.0, 0.001)
beta5~dnorm(0.0, 0.001)
beta6~dnorm(0.0, 0.001)
beta7~dnorm(0.0, 0.001)
beta8~dnorm(0.0, 0.001)
# O for Obesity
for (i in 1:N1){
O[i, 1:M] ~ dmnorm (mu1[], Omega[,] )
}
for (j in 1:M) {
mu1[j] <- beta1+beta2*time[j]
 }
Omega[1:M,1:M] ~ dwish (R [,],3)
Sigma [1:M,1:M] <- inverse(Omega[,])
# P for Pre Obesity
for (i in 1:N2) {
P[i, 1:M] ~ dmnorm (mu2[], Omega[,] )
}
for (j in 1:M) {
mu2[j] <- beta3+beta4*time[j]
 }
# N for Normal Weight
for (i in 1:N3) {
N[i, 1:M] ~ dmnorm (mu3[], Omega[,] )
}
for (j in 1:M) {
mu3[j] <- beta5+beta6*time[j]
 }
# U for Under weight
for (i in 1:N4) {
```

```
U[i, 1:M] ~ dmnorm (mu4[], Omega[,] )
}
for (j in 1:M) {
mu4[j] <- beta7+beta8*time[j]
 }
d13<-beta1-beta3
d15<-beta1-beta5
d17<-beta1-beta7
d35<-beta3-beta5
d37<-beta3-beta7
d57<-beta5-beta7
d24<-beta2-beta4
d26<-beta2-beta6
d28<-beta2-beta8
d46<-beta4-beta6
d48<-beta4-beta8
d68<-beta6-beta8
}
# initial values
list(beta1 = 0.5, beta2 = 0.5,beta3 = 0.5,beta4 = 0.5,
beta5= 0.5,
beta6 =0.5,beta7 =0.5,beta8 =0.5)
# Data( other information)
list(N1=1115, N2=1295, N3=844, N4=27, M=3,
time=c(1,2,3),
R=structure(.Data=c(1,0,0,0,1,0,0,0,1),.Dim=c(3,3)))
```