



Study of Biological Age and Chronological Age among Diabetes and Non-Diabetes: Case-Control Study

Mahendra M. Alate* and Satish V. Kakade

Department of Community Medicine, Krishna Institute of Medical Sciences, Krishna Vishwa Vidyapeeth (Deemed to be University), Karad – 415110, Maharashtra, India; mahendra.alate@gmail.com

Abstract

Background: Age is a gradual and irreversible pathophysiological process. There are two types of ages one is Chronological Age (CA) another is Biological Age (BA). CA starts from the date of birth and biological age indicates what current physical condition of the body of those persons. Overall in India, seventy-seven million people above the age of 18 years are surviving from diabetes and out of that almost twenty-five million are pre-diabetics. Diabetes mellitus is linked with an increased risk of serious health complications which decrease health span. Our area of interest study of BA and CA among diabetes and non-diabetes participants. **Aim:** Comparison of biological age and chronological age in diabetes and Non-diabetes Participants. **Material and Methods:** A Study was conducted in a pastoral area of western Maharashtra and collected data by house-to-house survey. Biological age was precise by using a standard instrument Omron HBF-375-IN Body Composition Monitor. We studied a total of 507 subjects, those aged 18 to 84 years, individuals with any surgical illness and physically handicapped were excluded. **Results:** We observed that 10.6% of people were suffering from diabetes out of 507. The Mean chronological age of diabetes mellitus participants was 64.85 ± 10.856 and 47.7 ± 16.17 for non-diabetes mellitus participants. The Biological age of diabetes mellitus participants was 62.75 ± 10.6 and 49.07 ± 14.94 of non-diabetes mellitus participants. The mean difference between the biological age and chronological age of diabetes mellitus participants was 2.1851 ± 9.37 and 1.25 ± 12.5477 in non-diabetes mellitus. The difference in these means was moderately significant ($t = 0.43489$, $p = 0.6645$). **Conclusions:** The Biological age of Non-diabetes Participants is less as compared to chronological age. Diabetes Participants have more biological ages as compared to their chronological age.

Keywords: Biological Age, Chronological Age, Diabetes and Non-diabetes Participant

1. Introduction

Age is a gradual and irreversible pathophysiological process¹. There are two types of ages one is CA another is BA. CA starts from the date of birth and BA indicates what current physical condition of the body of that person. The idea of Biological Age (BA) was first introduced in 1969¹. BA is based on changes in a cellular stage and it is robustly correlated with morbidity, mortality, and longevity².

There are several parameters needed to estimate BA, such parameters are called biomarkers.

Overall in India, 77 million people above the age of 18 years are surviving from diabetes and out of that almost 25 million are pre-diabetics. Diabetes mellitus correlates with an increased threat of serious fitness complications which decrease health span. Diabetes is renowned as a serious public health worry with a huge impact on human life and health expenditures. Nowadays economic

*Author for correspondence

developments as well as urbanization have led to a rising burden of diabetes in the world³. Alotaibi *et al.* suggested that have been raised that more than 1/3 of diabetes-related deaths occur in people below the age of sixty⁴.

Diabetes is not only associated with increased morbidity but also mortality. There are two types of diabetes. Type 1 Diabetes Mellitus (T1DM) also famous as Insulin Dependent Diabetes Mellitus (IDDM) is influenced by genetic and environmental factors⁵, resulting in the autoimmune destruction of β -cells responsible for the construction of insulin in the pancreas. Type 2 diabetes (T2DM) is a multi-factorial mess resulting from a mixture of multiple genetic factors allied to abnormal insulin secretion, insulin resistance and several environmental factors including physical immobility, pressure, obesity and aging^{6,7}.

In the 2020 report of the national vital statistics survey, over 30 million people are suffering from T2DM in the USA, out of them over 60 years old. Their hazard for mortality is 50% higher, and life expectancy is just about 5 years shorter as compared to non-diabetic persons. T2DM correlates with significant morbidity and increased risk of serious health complications such as blindness, kidney failure, heart infections, stroke, and amputations². There are several causes of T2DM deskbound lifestyle, genetic frame, food practice, physical movement and obesity.

Bahour *et al.* Conducted a study on the correlation of BA and CA in people suffering from Diabetes³. A total of 1798 persons were included in the research of clinical biomarkers that are notably correlated with CA. They have studied eight scientific biomarkers that are connected with CA in people without diabetes. BA was calculated using the Klemra and Doubal Method 1 (KDM1) as well as Multiple Linear Regression (MLR). The people suffering from T2DM had a typical age of 12.02 years higher than people without diabetes ($p < 0.0001$), while BA in T1DM was 16.32 years higher ($p < 0.0001$).

In this topic, a very limited review of the literature was observed, so our area of interest is to study the correlation of BA and CA among people suffering from diabetes in western Maharashtra.

2. Material and Methodology

A study was conducted in the pastoral area of western Maharashtra and collected data by house-to-house survey. Chronological Age, Biological age along with

gender, Diet, Education, Religion, Marital status, Economic status, Blood Pressure and Ophthalmological Problems were studied. Biological age was precise by using an ordinary instrument Omron HBF-375-IN Body Composition Monitor. A total of 54 subjects with diabetes aged between 18 to 84 years were identified in this study. Any further co-morbid medical/surgical infirmity and physical handicaps were barred.

2.1 Sample Size

Comparison of Diabetes and obesity with the help of the odds ratio of Body Mass Index {BMI} and comparison of Diabetes and Non-diabetes with the help of odds ratio of Hypertension⁸.

		Diabetes (338)	Non-diabetes (6322)	Odds Ratio
Hypertension	Yes	165	1458	3.18
	No	173	4864	
BMI	Yes	244	3051	2.78
	No	94	3271	

The sample size was calculated using the following formula:

$$n = \frac{Z^2_{1-\frac{\alpha}{2}} \left\{ \frac{1}{p_1(1-p_1)} + \frac{1}{p_2(1-p_2)} \right\}}{(\log_e(1-\epsilon))^2}$$

where, $Z^2_{1-\frac{\alpha}{2}}$ at 95% confidence Interval i.e. 1.96

$$p_1 = \text{the probability of exposure for people with disease} \\ = \frac{a}{a+b} = \frac{165}{165+1458} = 3.18$$

$$p_2 = \text{probability of exposure for people without disease} \\ \frac{c}{c+d} = \frac{3051}{3051+3271} = 2.78$$

ϵ = Precision

In this study of 507 individuals from rural areas, 54 were known to be diabetic. To fulfil the objective of the present study, the selection of non-diabetics was done in the ratio of 1:2. A Total of 108 age-sex matched non-diabetics were selected from 453 subjects. For each case, the age of control was matched with ± 2 yrs.

Sex		Non-diabetes Mellitus Participants	Diabetes Mellitus Participants	Chi-square value	p-value
	Male	66(61.1%)	33(61.1%)	0.000	1.000
Female	42 (38.9%)	21(38.9%)			

Age		n	Mean	SD	t value	p-value
	Non-diabetes Mellitus Participants	108	64.66	10.858	0.1050	0.107
Diabetes Mellitus Participants	54	64.85	10.858			

Table 1. Distribution of demographic variables

		Non-diabetes Mellitus Participants	Diabetes Mellitus Participants	Chi-square value	P value
Sex	Male	66(61.1)	33(61.1)	0.00	1
	Female	42(38.9)	21(38.9)		
Diet	Vegetarian	25(23.1)	7(13)	2.356	0.125
	Mix	83(76.9)	47(87)		
Education	Up to 10 Std	70(64.8)	34(63)	5.902	0.052
	11-12	18 (16.7)	16(29.6)		
	U.G. and P.G	20(18.4)	4(7.4)		
Religions	Hindu	90(83.3)	45(83.3)	1.688	0.430
	Muslim	3(2.8)	0		
	Others	15(13.9)	9(16.7)		
Economical status	AAY	2(1.9)	1(1.9)	0.282	0.896
	APL	93(86.1)	48(88.9)		
	BPL	13(20.0)	5(9.3)		
Bp	No	65(60.2)	23(42.6)	4.490	0.034
	Yes	43(39.8)	31(57.4)		
Ophthalmological problem	NO	94(87)	45(83.3)	0.405	0.524
	YES	14(13.0)	9(16.7)		
Marital status	Married	99(91.7)	44(81.5)	3.607	0.058
	Widow	9(8.3)	10(18.5)		

3. Statistical Analysis

Events were tabulated and analyzed using Statistical Package for Social Sciences (SPSS) version 28. The results were articulated in terms of descriptive statistics (frequency, percentage, mean and standard deviation). Facts were compared between two groups by unpaired t-test. The value of < 0.05 was considered statistically significant.

4. Results

In the current study, a comparison of chronological age and biological age was performed in both groups of Non-diabetes Mellitus and diabetes Mellitus Participants. Out of the total 507 subjects enrolled for the study. The mean (\pm SD) age of participants was 64 years. Among them, a female ($n = 21$, 38%) was observed with diabetes. The majority of them (34%) had primary education (which resources up to 10th standards), while 16% of them had

Table 2. Relation of CA and BA in non-diabetes mellitus participants

Non-diabetes Mellitus Participants					
	n	Mean	SD	t value	p-value
Age	108	64.66	10.85		
BA	108	60.13	10.98		
Difference of Age - BA	108	4.528	11.958	3.336	<0.001

Table 3. Relation of CA and BA in diabetes mellitus participants

Diabetes Mellitus Participants					
	n	Mean	SD	t-value	p-value
Age	54	64.85	10.858		
BA	54	62.76	10.602		
Difference of Age - BA	54	2.093	9.319	1.650	0.105

put higher secondary education. subsequently were those with graduate level education (4%) in diabetes surviving participants. Economically, 48% were from the below poverty line, 5% were below the poverty line and 1% were own business persons suffering from DM Whereas 93% were from above the poverty line, 13 % were below the poverty line and 2% were business persons non-diabetic. It means that slightly more than semi of the respondents belonged to the lower-middle-income group; 1/5th belonged to the low-income crowd. 83 % of persons preferred mixed types of food in both groups. There are some of the factors associated with BA and CA shown in Table 1.

A total of 507 participants were built-in in this study. The mean chronological age was 64.66 ± 10.85 and the mean biological age was 60.13 ± 10.98 among non-diabetes mellitus participants. Only 4.528 years of age difference in Non-diabetes mellitus participants that is they are five years younger than chronological age. The difference in chronological Age - BA among Diabetes Mellitus Participants is significant $p < 0.001$ (Table 2). The mean chronological age was 64.85 ± 10.858 and the mean Biological age was 62.76 ± 10.602 years among diabetes mellitus participants. Only 2.093 years of age difference in diabetes mellitus participants. There was in ± 2 year's age difference in biological among Non-diabetes mellitus participants and diabetes mellitus participants due to some clinical reasons.

The average of actual age and BA among non-diabetes mellitus participants was different, but there was no variation. However, there were statistically significant differences in chronological age and biological age

< 0.001 (Table 2). In general, a difference in chronological Age - BA among non-diabetes mellitus participants is significant $p < 0.001$.

BA was found to be lesser than chronological age in both groups, i.e., diabetic and non-diabetes participants. BA was significantly lesser than chronological age in diabetic and non-diabetes.

5. Discussion

In General, CA describes the years lived since birth. BA exclusively measures the rate of cellular turndown or physiological breakdown of cells and organs inside the body. CA can directly impact on BA³. BA is accelerated when compared to CA in diabetes mellitus.

In the present study, the mean chronological age of non-diabetes participants was 64.6 ± 10.85 while in the diabetes group was 64.85 ± 10.85 . This relationship was found to be not significant. The mean biological age among non-diabetic participants was 60.13 ± 10.98 also in the diabetes group was 62.76 ± 10.602 there was not statistically significant. Our results are similar to the study of La-or Chailurkit *et al*⁹. They found Chronological age was associated with incident diabetes but was not significant.

Hypertension is common among patients with DM with prevalence depending on types of DM, duration of DM, age, sex and BMI¹⁰. Hypertension is double as frequent in patients with diabetes compared with those who do not have Diabetes¹¹. BA metrics are associated with lifestyle factors and health scores that in turn are related to hypertension rate¹²⁻¹⁹. To our sequence, no eventual study

has openly examined the link between biological age and incident hypertension. *Kresovich et al.* conducted a study on methylation-based biological age and hypertension prevalence and incidence. They establish that all three BA metrics were higher among women who went on to be diagnosed with hypertension suggesting that increases in biological age occur in the years earlier the scientific onset of hypertension²⁰.

Chen *et al.* studied 5278 people with diabetes from the Survey of the National Health and Nutrition Examination. Biological ageing was positively related to mortality among people with diabetes²¹. This study carried out, a significant relation in BA and CA among DM and Non DM respectively.

6. Conclusions

Non-diabetic participants are younger than participants surfing diabetes. Moderate education, absence of raised BP and staying with a spouse are the major factors which keep individuals younger in the non-diabetic population compared to the diabetic population.

7. Acknowledgement

The authors are thankful to the team of our rich and extension activity of Krishna Vishwa Vidyapeeth (Deemed to be University), Karad for collating data. I especially give my thanks to Dr. S.V. Kakade for supporting statistical knowledge, and statistical analysis.

8. References

- Guo J, Huang X, Dou L, Yan M, Shen T, Tang W, *et al.* Aging and aging-related diseases: From molecular mechanisms to interventions and treatments. *Signal Transduct Target Ther.* 2022; 7(1):391. <https://doi.org/10.1038/s41392-022-01251-0> PMID:36522308 PMCid:PMC9755275
- Comfort A. Test-battery to measure ageing-rate in man. *The Lancet.* 1969; 294(7635):1411-5. [https://doi.org/10.1016/S0140-6736\(69\)90950-7](https://doi.org/10.1016/S0140-6736(69)90950-7) PMID:4188291
- Bahour N, Cortez B, Pan H, Shah H, Doria A, Aguayo-Mazzucato C. Diabetes mellitus correlates with increased biological age as indicated by clinical biomarkers. *Geroscience.* 2022;1-3. <https://doi.org/10.1007/s11357-021-00469-0> PMID:34773197 PMCid:PMC8589453
- Khan MAB, Hashim MJ, King JK, Govender RD, Mustafa H, Al Kaabi J. Epidemiology of type 2 diabetes-global burden of disease and forecasted trends. *J Epidemiol Glob Hea.* 2020; 10(1):107-11. <https://doi.org/10.2991/jegh.k.191028.001> PMID:32175717 PMCid:PMC7310804
- Alotaibi A, Perry L, Gholizadeh L, Al-Ganmi A. Incidence and prevalence rates of diabetes mellitus in Saudi Arabia: An overview. *J Epidemiol Glob Health.* 2017; 7:211-18. <https://doi.org/10.1016/j.jegh.2017.10.001> PMID:29110860 PMCid:PMC7384574
- Siddiqui AA, Siddiqui SA, Ahmad S, Siddiqui S, Ahsan I, Sahu K. Diabetes: Mechanism, pathophysiology and management-A review. *Int J Drug Dev Res.* 2013; 5(2):1-23.
- Yaribeygi H, Farrokhi FR, Butler AE, Sahebkar A. Insulin resistance: Review of the underlying molecular mechanisms. *J Cell Physiol.* 2019; 234(6):8152-61. <https://doi.org/10.1002/jcp.27603> PMID:30317615
- Agrawal S, Millett CJ, Dhillon PK, Subramanian SV, Ebrahim S. Type of vegetarian diet, obesity and diabetes in adult Indian population. *Nutr J.* 2014; 13:89. <https://doi.org/10.1186/1475-2891-13-89> PMID:25192735 PMCid:PMC4168165
- Chailurkit LO, Thongmung N, Vathesatogkit P, Sritara P, Ongphiphadhanakul B. Biological age as estimated by baseline circulating metabolites is associated with incident diabetes and mortality. *J Nutr Health Aging.* 2024:100032. <https://doi.org/10.1016/j.jnha.2023.100032> PMID:38388109
- Khazaei HA, Teymuri B, Nakhaei A, Mohammadi M, Noura M, Khazaei A, *et al.* Evaluation of haptoglobin phenotypes in association with clinical features of patients suffered from preterm labor disease. *Acta Med Iran.* 2014; 52(2):106-10. PMID: 24659066.
- Petrie JR, Guzik TJ, Touyz RM. Diabetes, hypertension, and cardiovascular disease: Clinical insights and vascular mechanisms. *Can J Cardiol.* 2018; 34(5):575-84. <https://doi.org/10.1016/j.cjca.2017.12.005> PMID:29459239 PMCid:PMC5953551
- Lemke E, Vetter VM, Berger N, Banszerus VL, Konig M, Demuth I. Cardiovascular health is associated with the epigenetic clock in the Berlin Aging Study II (BASE-II). *Mech Ageing Dev.* 2022; 201:111616. <https://doi.org/10.1016/j.mad.2021.111616> PMID:34879249
- Pottinger TD, Khan SS, Zheng Y, Zhang W, Tindle HA, Allison M, *et al.* Association of cardiovascular health and epigenetic age acceleration. *Clin Epigenetics.* 2021; 13:42. <https://doi.org/10.1186/s13148-021-01028-2> PMID:33632308 PMCid:PMC7905851
- Joyce BT, Gao T, Zheng Y, Ma J, Hwang SJ, Liu L, *et al.* Epigenetic age acceleration reflects long-term cardiovascular health. *Circ Res.* 2021; 129:770-81. <https://doi.org/10.1161/CIRCRESAHA.121.318965> PMID:34428927 PMCid:PMC8484046

15. Nannini DR, Joyce BT, Zheng Y, Gao T, Liu L, Yoon G, *et al.* Epigenetic age acceleration and metabolic syndrome in the coronary artery risk development in young adults study. *Clin Epigenetics.* 2019; 11:160. <https://doi.org/10.1186/s13148-019-0767-1> PMID:31730017 PMCID:PMC6858654
16. Ammous F, Zhao W, Ratliff SM, Mosley TH, Bielak LF, Zhou X, *et al.* Epigenetic age acceleration is associated with cardiometabolic risk factors and clinical cardiovascular disease risk scores in African Americans *Clin Epigenetics.* 2021; 13:55. <https://doi.org/10.1186/s13148-021-01035-3> PMID:33726838 PMCID:PMC7962278
17. Kresovich JK, Lopez AMM, Garval EL, Xu Z, White AJ, Sandler DP, *et al.* Alcohol consumption and methylation-based measures of biological age. *J Gerontol: Series A.* 2021; 76:2107-11. <https://doi.org/10.1093/gerona/glab149> PMID:34038541 PMCID:PMC8599006
18. Kresovich JK, Park YM, Keller JA, Sandler DP, Taylor JA. Healthy eating patterns and epigenetic measures of biological age. *Am J Clin Nutr.* 2022; 115:171-9. <https://doi.org/10.1093/ajcn/nqab307> PMID:34637497 PMCID:PMC8754996
19. Kresovich JK, Garval EL, Lopez AMM, Xu Z, Niehoff NM, White AJ, *et al.* Associations of body composition and physical activity level with multiple measures of epigenetic age acceleration. *Am J Epidemiol.* 2021; 190:984-93. <https://doi.org/10.1093/aje/kwaa251> PMID:33693587 PMCID:PMC8168202
20. Kresovich JK, Sandler DP, Taylor JA. Methylation-based biological age and hypertension prevalence and incidence. *Hypertension.* 2023; 80(6):1213-22. <https://doi.org/10.1161/HYPERTENSIONAHA.122.20796> PMID:36974720 PMCID:PMC10192055
21. Chen L, Yin X, Zhao Y, Chen H, Tan T, Yao P, *et al.* Biological ageing and the risks of all-cause and cause-specific mortality among people with diabetes: a prospective cohort study. *J Epidemiol Community Health.* 2022; 76(9):771-8. <https://doi.org/10.1136/jech-2022-219142> PMID:35738895