

# The Difference in Risk Factors Between Adults With Early-Onset (<40 Years Old) Versus Late-Onset (≥40 Years Old) Type 2 Diabetes in a University Hospital From January 2015-December 2017



Marilyn Katrina C. Caro, MD, Elaine C. Cunanan, MD, MHPEd

## ABSTRACT

**Background:** Diabetes will remain a threat to global health. No longer just a disorder of mature age, there is now a well-recognized trend towards the young. Early diagnosis leads to early intervention and prevention of complications in this susceptible but vital portion of the population.

**Objective:** To compare the risk factors predisposing adults to early-onset (<40 years old) versus late-onset (≥40 years old) type 2 diabetes at the University of Santo Tomas Hospital from January 2015-December 2017.

**Methods:** This is a retrospective review of medical records. All adult patients who fulfilled the inclusion criteria from January 2015 to December 2017 were included in the study. Data from charts were reviewed and analyzed.

**Results:** The early-onset group had a mean age of 34 years, while the late-onset group had a mean age of 51 years. The early-onset diabetics were mostly obese, had higher HbA1c, worse lipid profiles, and had a positive family history of diabetes. Only a BMI of >27.50 kg/m<sup>2</sup> was found to be a significant

risk factor contributing to early-onset of diabetes. Myocardial infarction and nephropathy were more frequent in the late-onset group while retinopathy was more common in the early-onset group. Lastly, only retinopathy and neuropathy were significantly associated with longer duration of diabetes.

**Conclusion:** The mean age of Filipinos was at least 5 years younger than the studies done on Caucasians. Most patients in the early-onset group were obese and had worse metabolic profiles. Retinopathy was more common in the early-onset group, while myocardial infarction and neuropathy were more common in the latter.

**Key words:** risk factors, early-onset diabetes, Philippines

## INTRODUCTION

Diabetes mellitus is a group of metabolic disorders characterized by a deficiency of insulin secretion and/or insulin effect, which causes hyperglycemia, disturbance of carbohydrate, fat, and protein metabolism, and a constellation of chronic complications. Diabetes will remain a threat to global health. Worldwide, diabetes probably affects 150 million people. The International Diabetes Federation estimated that almost 60% of newly diagnosed diabetics will be in Asia. The global

✉ Marilyn Katrina C. Caro, MD  
marikatcastcar@gmail.com

Section of Endocrinology, Diabetes and Metabolism,  
The Department of Medicine, University of Santo Tomas  
Hospital, Manila, Philippines

burden of type 2 diabetes is significant and rising. While most of the increase in its prevalence occurs in the middle-aged and elderly, it is becoming more common in younger patients. In fact, there is now a well-recognized trend toward younger people presenting with the disease, particularly for some ethnic groups.

Based on diabetes landmark trials, the occurrence of diabetes in younger individuals is directly associated with its complications, thus, longer exposure to hyperglycemia and other diabetes-related abnormalities increases the likelihood that patients will develop complications.

There is a paucity of local studies comparing risk factors between adults with early-onset versus late-onset type 2 diabetes. Hence, further investigation of the characteristics of these young individuals is vital in order to prevent the burden of its complications.

## METHODOLOGY

This study was conducted in compliance with the ethical principles of medical research involving human subjects under the Declaration of Helsinki by the World Medical Association in 2013 and the National Ethical Guidelines for Health and Health-Related Research 2017 Edition. The USTH-REC approved this study before commencement.

This was a retrospective review of medical records of adult patients with type 2 diabetes who were seen at the outpatient department of the University of Santo Tomas Hospital, from January 2015 to December 2017. Subjects with type 1 diabetes, monogenic diabetes, and latent autoimmune diabetes of adulthood were excluded. Data collection was from May 15 to October 30, 2018. Data obtained from the chart included date of diagnosis, age of onset of diabetes, gender, race, height, body weight, family history of diabetes, gestational diabetes if female, and other comorbid conditions. Blood pressure was also recorded along with results of HbA1c, lipid profile, micral test, and serum creatinine. Fundoscopy and monofilament test findings were also recorded. Subjects were divided into two groups based on age at diagnosis: early-onset (<40 years of age) and late-onset ( $\geq$ 40 years of age). Two independent persons reviewed the chart and compared the results. Data retrieved was tabulated and analyzed as to baseline characteristics, risk factors, and identified end-organ complications. The

odds of acquiring diabetes-related complications with the duration of diabetes as a risk factor were also estimated.

A purposive sampling design was used to select study participants. Although the minimum sample size of 120 records was necessary to achieve a power of 80% with a medium effect size of 0.50 at an alpha of 0.05, 200 medical records were reviewed. Out of the initial records, 120 had complete information based on variables included in the data collection form; of which, 44 subjects comprised the early-onset group while 76 subjects encompassed the late-onset cluster. Comparative analysis of the mean values of continuous variables between the two groups was analyzed using the independent sample t-test. If however statistical assumptions were not met, then the Mann-Whitney test was used. Categorical variables on the other hand were analyzed using the chi-square test. Logistic regression analysis was used to determine the association of duration of diabetes as a risk factor for both macrovascular and microvascular complications in adults with early-onset and late-onset type 2 diabetes. All statistical tests were done in SPSS version 20.0. P-values less than 0.05 were considered significant.

## Operational Definition of Terms

In this study, early-onset type 2 diabetes was defined as adults who were diagnosed with type 2 diabetes below 40 years old as stipulated in the National Institute for Health and Care Excellence (NICE) guideline. Moreover, a positive family history of diabetes was defined as having at least one first degree or second degree relative with diabetes. Overweight and obese adults were defined as having a body mass index of 23-24.9 kg/m<sup>2</sup>, and >25 kg/m<sup>2</sup>, respectively according to the Asia Pacific criteria. Dyslipidemia was defined as having a total cholesterol  $\geq$ 200 mg/dL, triglycerides of  $\geq$ 150 mg/dL, LDL cholesterol of  $\geq$ 100 mg/dL, and HDL cholesterol of <50 mg/dL in females and <40 mg/dL in males. In addition, hypertension was defined as systolic or diastolic blood pressure of more than or equal to 140 mmHg or more than or equal to 90 mmHg respectively, or who have received treatment for hypertension. Macrovascular complications recorded in the study included a history of myocardial infarction or stroke. On the contrary, microvascular included evidence of retinopathy, neuropathy

(pertinent physical exam findings), and nephropathy (elevated creatinine).

## RESULTS

### Demographics and Baseline Characteristics

Table 1 summarizes the demographic and clinical profile of the early-onset group as compared to the latter. The mean age for the early-onset group was 34 years, while that of the late-onset group was 51 years. There was no gender predilection between the two groups. Most early-onset respondents were obese (47.73%), had light physical activities (54.55%), were non-smokers (79.55%), and had a BP of less than 140/90 (88.64%). Furthermore, 86.36% of the early-onset group had a positive family history of diabetes, and 22.73% of females had a history of gestational diabetes mellitus. Their lipid profile showed elevated triglycerides (59.09%) and LDL (81.82%) with low HDL for both males (36.6%) and females (38.63%), respectively. The average duration of diabetes upon first visit was 3.26 ( $\pm 2.84$ ) years. More importantly, 79.55% had an HbA1c of  $>7\%$ . The most common comorbid illnesses were hypertension (27.7%) followed by dyslipidemia (9.09%), polycystic ovarian syndrome (6.81%), fatty liver (4.54%), and metabolic syndrome (4.54%).

### Risk Factors for Early-onset Type 2 Diabetes

Table 2 illustrates the comparative analysis of risk factors associated with the development of diabetes between the two groups. Among these, only a BMI of  $>27.50 \text{ kg/m}^2$  (obese) ( $p < 0.05$ ) was statistically different between the two groups, such that the proportion of patients who were obese was statistically higher among subjects with the early-onset group (47.73%) compared to the latter (27.63%). Moreover, the early-onset group had statistically higher mean HbA1c of 10.25 (2.23), statistically higher triglyceride levels at 260.14 ( $\pm 167.64$ ), and statistically lower HDL at 35.25 ( $\pm 12.55$ ) than the late-onset group with values of 8.93 (2.45), 163.87 ( $\pm 54.20$ ), and 45.05 ( $\pm 13.28$ ), respectively.

### Frequency of Macrovascular and Microvascular Complications in Early-Onset Diabetics

Table 3 compared the frequency of microvascular and macrovascular complications between the two

groups. The results showed that the proportion of myocardial infarction was significantly higher among the late-onset group (38.16%). In terms of microvascular complications, statistically significant retinopathy was present in 47.72% of patients in the early-onset group and 23.68% in the late-onset group.

### Influence of Disease Duration on Macrovascular and Microvascular Complications in Early-Onset Diabetics

Table 4 revealed the correlation of diabetes duration to macrovascular and microvascular complications. In this study, only microvascular complications were significantly associated with diabetes duration. Hence for every 1 year increase in the duration of diabetes, the subjects are 11% and 29% more likely to develop retinopathy and neuropathy, respectively.

## DISCUSSION

In this study, mean age for the early-onset group was 34, while that of the late-onset group was 51 years. This was similar to the studies done by Kim, et al.[1] and Jimenez-Corona, et al.[2] in 2010. However, the results of this study showed that the mean age of Filipinos for both groups was at least 5 years younger than the studies done on Asians and Caucasians. Moreover, there was no gender predilection between the two groups. This was similar to a study by Huo, et al.,[3] which proposed that the prevalence of diabetes was similar in males and females. Furthermore, the early-onset group's level of physical activity was mostly sedentary (25.0%) to light (54.55%). This was compatible with studies establishing that a sedentary lifestyle had a major impact on the development of disease.[1] In addition, a study by Hitke, Webb, Jhunti, et al. in 2015[4] and Yu, et al. in 2016[5] showed that early-onset subjects were mostly obese. Indeed, among the risk factors, only an obese BMI was found to be significantly higher in the early-onset group. This reflects the close association between obesity and insulin resistance. Obesity itself is an independent risk factor for diabetes such that there is a seven-fold and three-fold increased risk of developing diabetes in the obese and overweight, respectively.[4,5] With regard to family history, Kim, et al.[1] reported that diabetes occurred earlier in persons who had

**Table 1.** Clinical Profile of the Respondents According to Onset of Diabetes Mellitus (N = 120)

Characteristics	Onset of Diabetes Mellitus	
	Early-Onset (n = 44)	Late-Onset (n = 76)
<b>Age</b>	33.8 (4.16)	51 (8.7)
<b>Sex</b>		
Male	22 (50.00%)	36 (47.37%)
Female	22 (50.00%)	40 (52.63%)
<b>Height (centimeters)</b>	163.32 ( $\pm$ 8.07)	163.68 ( $\pm$ 6.50)
<b>Weight (kilograms)</b>	74.76 ( $\pm$ 17.64)	69.03 ( $\pm$ 11.81)
<b>BMI (kg/m<sup>2</sup>)</b>		
Less than 18.50 kg/m <sup>2</sup>	1 (2.27%)	1 (1.32%)
Between 18.50 kg/m <sup>2</sup> to 23.00 kg/m <sup>2</sup>	10 (22.73%)	20 (26.32%)
Between 23.00 kg/m <sup>2</sup> to 27.50 kg/m <sup>2</sup>	12 (27.27%)	34 (44.74%)
$\geq$ 27.50 kg/m <sup>2</sup>	21 (47.73%)	21 (27.63%)
<b>Level of Physical Activity</b>		
Sedentary	11 (25.00%)	9 (11.84%)
Light	24 (54.55%)	56 (73.68%)
Moderate	9 (20.45%)	10 (13.16%)
Vigorous	0 (0.00%)	1 (1.32%)
<b>Duration of Diabetes Mellitus (Years)</b>	3.26 ( $\pm$ 2.84)	6.70 ( $\pm$ 4.10)
<b>Family History of Diabetes Mellitus</b>	38 (86.36%)	58 (76.32%)
<b>History of Gestational Diabetes Mellitus (if female)</b>	10 (22.73%)	17 (22.37%)
<b>Blood Pressure (mmHg)</b>		
<140/90	39 (88.64%)	26 (34.21%)
$\geq$ 140/90	5 (11.36%)	50 (65.79%)
<b>HbA1c (%)</b>		
<7.0%	9 (20.45%)	11 (14.47%)
$\geq$ 7.0%	35 (79.55%)	65 (85.53%)
<b>Total Cholesterol (mg/dL)</b>		
<200.00 mg/dL	22 (50.00%)	25 (32.89%)
$\geq$ 200.00 mg/dL	22 (50.00%)	51 (67.11%)
<b>Triglycerides (mg/dL)</b>		
<150.00 mg/dL	18 (40.91%)	25 (32.89%)
$\geq$ 150.00 mg/dL	26 (59.09%)	51 (67.11%)
<b>HDL (mg/dL)</b>		
<50 mg/dL	16 (36.6%)	21 (27.63%)
$\geq$ 50 mg/dL	6 (13.64%)	15 (19.73%)
<60 mg/dL	17 (38.63%)	38 (50.0%)
$\geq$ 60 mg/dL	3 (6.81%)	3 (3.94%)
<b>LDL (mg/dL)</b>		
<100.00 mg/dL	8 (18.18%)	6 (7.89%)
$\geq$ 100.00 mg/dL	36 (81.82%)	70 (92.11%)

**Table 1.** Clinical Profile of the Respondents According to Onset of Diabetes Mellitus (N = 120) (Continued)

Characteristics	Onset of Diabetes Mellitus	
	Early-Onset (n = 44)	Late-Onset (n = 76)
<b>Serum Creatinine (mg/dL)</b>	1.04 (±1.10)	1.09 (±0.60)
<b>Comorbidities</b>		
Hypertension	12 (27.7%)	49 (64.47%)
Fatty Liver	2 (4.54%)	3 (3.94%)
PCOS	3 (6.81%)	0 (0.00%)
Dyslipidemia	4 (9.09%)	11 (14.47%)
Metabolic Syndrome	2 (4.54%)	1 (1.31%)

**Table 2.** Comparative Analyses of the Risk Factors Between Respondents With Early and Late-Onset Diabetes Mellitus (N = 120)

Risk Factors	Mean (SD) or Frequency (Percentage) <sup>a</sup>		p-value <sup>b</sup>
	Early-onset (n = 44)	Late-onset (n = 76)	
<b>Gender</b>			0.781
Male	22 (50.00%)	36 (47.37%)	
Female	22 (50.00%)	40 (52.63%)	
<b>BMI (kg/m<sup>2</sup>)</b>			
Less than 18.50 kg/m <sup>2</sup>	1 (2.27%)	1 (1.32%)	0.6954
Between 18.50 kg/m <sup>2</sup> to 23.00 kg/m <sup>2</sup>	10 (22.73%)	20 (26.32%)	0.6616
Between 23.00 kg/m <sup>2</sup> to 27.50 kg/m <sup>2</sup>	12 (27.27%)	34 (44.74%)	0.0579
≥27.50 kg/m <sup>2</sup>	21 (47.73%)	21 (27.63%)	0.0261*
<b>Sedentary Lifestyle</b>	11 (25.00%)	9 (11.84%)	0.0623
<b>Family History of Diabetes Mellitus</b>	38 (86.36%)	58 (76.32%)	0.1852
<b>History of Gestational Diabetes Mellitus</b>	10 (22.73%)	17 (22.37%)	0.9637
<b>HbA1c</b>	10.25 (±2.23)	8.93 (±1.70)	0.0004†
<b>Lipid Profile</b>			
Total Cholesterol	208.36 (±49.12)	216.12 (±54.34)	0.4371
LDL	123.93 (±38.97)	137.75 (±40.14)	0.0688
HDL	35.25 (±12.55)	45.05 (±13.28)	0.0363
Triglycerides	260.14 (±167.64)	163.87 (±54.20)	0.0491

<sup>a</sup>Values are presented as mean (±SD) unless otherwise indicated.

<sup>b</sup>Comparative analyses were conducted using  $\chi^2$  or an independent t-test. If expected values were less than 5.00, Fisher’s Exact Test was used instead of  $\chi^2$ .

\*Significant at 0.05

†Significant at 0.01

a positive family history of the disease. A similar study done in India[6] had the same conclusion. This was consistent with the results of this study which showed that 86.36% of the early-onset group had a positive family history. Furthermore, the study by Yu H, et al. in 2016[5] elaborated that a history of gestational diabetes had a 10-fold increased risk of

developing diabetes after a 10-year follow-up. This study was at par with this deduction since 22.73% of the early-onset group and 22.37% of the latter had a history of gestational diabetes. It was also noted by Yang, et al.[7] that early-onset diabetics had a higher prevalence of diastolic hypertension (37% versus 26%, p<0.001) but a lower prevalence

**Table 3.** Comparative Analyses of the Macrovascular and Microvascular Complications Between Respondents With Early and Late-Onset Diabetes Mellitus (N = 120)

Complications	Frequency (Percentage) or Mean (SD)		$\chi^2$ -value or t-value	p-value
	<40 Years Old (n = 44)	≥40 Years Old (n = 76)		
<b>Macrovascular Complications</b>				
Stroke	2 (4.55%)	7 (9.21%)	0.87	0.483
Myocardial Infarction	1 (2.27%)	15 (19.73%)	7.35	0.006
<b>Microvascular Complications</b>				
Retinopathy	21 (47.72%)	18 (23.68%)	7.34*	0.0067
Neuropathy	2 (4.55%)	29 (38.16%)	16.43†	0.0001
Nephropathy				
Positive Micral Test	12 (27.27%)	33 (43.42%)	3.10	0.078
Serum Creatinine	1.04 (±1.10)	1.09 (±0.60)	-0.30	0.7667

<sup>a</sup>Values are presented as mean (±SD) unless otherwise indicated.

<sup>b</sup>Comparative analyses were conducted using  $\chi^2$  or independent t-test. If expected values were less than 5.00, Fisher's Exact test was used instead of  $\chi^2$ .

\*Significant at 0.05; †Significant at 0.01

**Table 4.** Binary Logistic Regression on the Influence of Duration of Diabetes Mellitus on Macrovascular and Microvascular Complications of Respondents (N = 120)

Outcome Variables	Duration of Diabetes Mellitus (Years)			
	Odds Ratio	Standard Errors	95% CI	p-value (two-tailed)
<b>Macrovascular Complications</b>				
Stroke	1.11	0.09	0.95 – 1.29	0.203
Myocardial Infarction	1.13	0.08	0.98 – 1.30	0.090
<b>Microvascular Complications</b>				
Retinopathy	1.11*	0.05	1.01 – 1.23	0.026
Neuropathy	1.29†	0.08	1.15 – 1.45	0.0001

\*Significant at 0.05

†Significant at 0.01

of systolic hypertension than late-onset diabetics. Indeed, systolic hypertension was higher in the late-onset group (34.21%) in the study. In relation to this, a study by Song, et al.[8] in 2008 presented that a significantly greater proportion of the early-onset group had hypertension (80%) and more adverse dyslipidemia (82%). This is congruent with our results wherein among the early-onset group, 81% had high LDL, 59% had high triglycerides, and 37% had low HDL indicating that more than half of the subjects from the early-onset group had dyslipidemia upon diagnosis. Moreover, in this study, the early-onset group had statistically higher triglycerides and statistically lower HDL as compared to the latter.

These results complemented the conclusions from the American, European, and Asian studies, which showed that diabetics diagnosed before the age of 40 years had worse lipid profiles than their late-onset counterparts.[9-11] More importantly, in this study, 79.9% of the early-onset group had HbA1c levels >7.0. This was parallel with the study done by Yu, et al.[5] wherein the early-onset group had worse glycemic control (HbA1c 7.7% versus 7.5%,  $p < 0.05$ ) than the late-onset group. More so, a study by Park, et al. in 2006[12] done on diabetics <30 years old revealed that HbA1c levels upon diagnosis were higher in the early-onset group and upon 6.8-year follow-up. This was similar to the results of this

study wherein the mean HbA1c for the early-onset group was 10.25 ( $\pm 2.23$ ), which was statistically higher than the late-onset group (Table 2). An elevated HbA1c denotes an increased risk of having macrovascular and microvascular complications creating the proposed adverse milieu for the early-onset group. Lastly, in the early-onset group, 6.81% had polycystic ovarian syndrome. This was consistent with the study done by Hitke, Webb, Jhunti, et al. in 2015[4] wherein features of metabolic syndrome due to insulin resistance and associated diseases such as polycystic ovarian syndrome were also documented in their early-onset subjects.

A study by Hillier in 2003[13] showed a twofold increase in the proportion of myocardial infarction in both early- and late-onset groups. This was compatible with results of the study wherein the proportion of myocardial infarction was significantly higher among the late-onset group (38.16%). Meanwhile, an observational study by Yokohama in 1997[14] showed that around 15% of Japanese adults diagnosed with type 2 diabetes less than 30 years old developed proliferative retinopathy. A retrospective study in different Asian countries[15] reported a greater prevalence of retinopathy and neuropathy among those with early-onset diabetes. This signifies that age may be an independent risk factor for both diabetic retinopathy and neuropathy. However, results of our study showed no significant difference in the proportion of retinopathy and nephropathy between the early- and late-onset group. This inference could be explained by the small sample size included in this study.

Lastly, in this study only microvascular complications were significantly associated with diabetes duration. The Diabcare-Asia study reported a 7% higher risk of macrovascular diseases for every year increase in age of diagnosis. However, this study did not show significant association between disease duration and macrovascular complications in both groups. This inference could be due to small sample size of the study. Thus, poor insight of the disease, modest health-seeking behavior, and lack of support system in the early-onset group are possible reasons that lead to suboptimal blood glucose control and development of microvascular complications, hence early screening is advocated.

## CONCLUSION

The mean age upon diagnosis was 33 for the early-onset group, and 52 for the late-onset group without gender and ethnic predilection. Most patients in the early-onset group were obese, had light physical activity, and had a family history of diabetes. Moreover, they had higher levels of HbA1c, higher triglycerides, and lower HDL levels upon diagnosis. The most common comorbidity in both groups was hypertension. Among the risk factors listed, only a BMI greater than 27.50 kg/m<sup>2</sup> (obese) ( $p < 0.05$ ) was statistically different between the two groups. Among the macrovascular and microvascular complications, a higher proportion of the late-onset group had a history of myocardial infarction. Retinopathy was more common in the early-onset group while prevalence of neuropathy was higher in the late-onset group. Lastly, the duration of diabetes was only associated with microvascular complications in both groups, such that for every year increase in the duration of diabetes, subjects were more likely to develop retinopathy and neuropathy.

## LIMITATIONS OF THE STUDY

The study was limited to a single tertiary care institution hence the sample size was relatively small. The small sample size could explain the lack of statistical power to account for some of the findings. Being a cross-sectional study, the study was unable to measure the exposure period of risk factors and how they contributed to disease progression. Moreover, being a retrospective study, the data collected was limited only to available information written on the patient's records. Thus, data that was not found in records were not included in the study.

## RECOMMENDATIONS

Thus, the study should be conducted within a longer time frame (2013-2017) in order to include and evaluate more complications of diabetes (eg, nephropathy) that usually develops within 5 years from diagnosis. Moreover, a study should be initiated that would correlate the association/effect of the risk factors on the early-onset group to provide predictors

of disease. Furthermore, commence a community-based study to increase the patient population and provide more diverse outcomes, and lastly investigate the endpoints of mortality, amputations, blindness, and dialysis in this early-onset subset.

#### **Disclosure and Conflict of Interest**

There are no conflict of interests that may inappropriately influence bias in the execution of research and publication of this manuscript.

#### **Acknowledgment**

Special gratitude is given to the University of Santo Tomas Hospital, Department of Medicine Research Committee, and to the Medical Records Department of the USTH. To all patients to whom this work is dedicated and ultimately to the Lord God, the Creator and Giver of Life, to whom we owe everything.



## REFERENCES

- Kim KS, Oh HJ, Kim JW, Lee YK, Kim SK, Park SW, et al. The clinical characteristics of the newly diagnosed early-onset (<40 years old) diabetes in outpatients' clinic. *Korean Diabetes J* [Internet]. 2010;34(2):119. Available from: <http://dx.doi.org/10.4093/kdj.2010.34.2.119>
- Jiménez-Corona A, Rojas R, Gómez-Pérez FJ, Aguilar-Salinas CA. Early-onset type 2 diabetes in a Mexican survey: results from the National Health and Nutrition Survey 2006. *Salud pública Méx* [Internet]. 2010;52:S27–35. Available from: <http://dx.doi.org/10.1590/s0036-36342010000700006>
- Huo X, Gao L, Guo L, Xu W, Wang W, Zhi X, et al. Risk of non-fatal cardiovascular diseases in early-onset versus late-onset type 2 diabetes in China: a cross-sectional study. *The Lancet Diabetes & Endocrinology* [Internet]. 2016 Feb;4(2):115–24. Available from: [http://dx.doi.org/10.1016/S2213-8587\(15\)00508-2](http://dx.doi.org/10.1016/S2213-8587(15)00508-2)
- Htike ZZ, Webb D, Khunti K, Davies M. Emerging epidemic and challenges of type 2 diabetes in young adults. *Diabetes Management* [Internet]. 2015 Nov;5(6):473–83. Available from: <http://dx.doi.org/10.2217/dmt.15.39>
- Yu H, Xie L-F, Chen K, Yang G-Y, Xing X-Y, Zhao J-J, et al. Initiating characteristics of early-onset type 2 diabetes mellitus in Chinese patients. *Chinese Medical Journal* [Internet]. 2016 Apr 5;129(7):778–84. Available from: <http://dx.doi.org/10.4103/0366-6999.178959>
- Vijayakumar G, Sreehari GK, Vijayakumar A, Jaleel A. Distinct predictors and comorbidities in early-onset type 2 diabetes mellitus among Asian Indians. *Metabolic Syndrome and Related Disorders* [Internet]. 2017 Nov;15(9):458–64. Available from: <http://dx.doi.org/10.1089/met.2017.0047>
- Yang W, Cai X, Han X, Ji L. Clinical characteristics of young type 2 diabetes patients with atherosclerosis. Feng YM, editor. *PLoS ONE* [Internet]. 2016 Jul 8;11(7):e0159055. Available from: <http://dx.doi.org/10.1371/journal.pone.0159055>
- Song SH, Hardisty CA. Early-onset type 2 diabetes mellitus: a harbinger for complications in later years—clinical observation from a secondary care cohort. *QJM* [Internet]. 2009 Sep 4;102(11):799–806. Available from: <http://dx.doi.org/10.1093/qjmed/hcp121>
- Chowdhury TA. Complications and cardiovascular risk factors in South Asians and Europeans with early-onset type 2 diabetes. *QJM* [Internet]. 2002 Apr 1;95(4):241–6. Available from: <http://dx.doi.org/10.1093/qjmed/95.4.241>
- Song SH. Review: Early-onset type 2 diabetes mellitus: a condition with elevated cardiovascular risk? *Diabetes & Vascular Disease* [Internet]. 2008 Mar;8(2):61–5. Available from: <http://dx.doi.org/10.1177/14746514080080020201>
- Deconinck B, Mathieu C, Benhalima K. Characteristics and cardiovascular complications of a large cohort of adults diagnosed with type 2 diabetes <45 years. *Diabetol Metab Syndr* [Internet]. 2017 May 2;9(1). Available from: <http://dx.doi.org/10.1186/s13098-017-0227-z>
- Park M, Kang YI, Chon S, Oh SJ, Woo JT, Kim SW, et al. The clinical characteristics of young onset diabetes according to etiology based classification. *J Korean Diabetes Assoc.* 2006;30:190–97.
- Hillier TA, Pedula KL. Complications in young adults with early-onset type 2 diabetes. *Diabetes Care* [Internet]. 2003 Nov 1;26(11):2999–3005. Available from: <http://dx.doi.org/10.2337/diacare.26.11.2999>
- Yokoyama H, Okudaira M, Otani T, Takaike H, Miura J, Saeki A, et al. Existence of early-onset NIDDM Japanese demonstrating severe diabetic complications. *Diabetes Care.* 1997 May;20(5):844–7. doi: 10.2337/diacare.20.5.844. PMID: 9135953.
- Reddy NG, Venkatesh R, Jayadev C, Gadde SGK, Agrawal S, Mishra P, et al. Diabetic retinopathy and diabetic macular edema in people with early-onset diabetes. *Clin Diabetes.* 2022 Spring;40(2):222–32. doi: 10.2337/cd21-0110. Epub 2022 Apr 15. PMID: 35669299; PMCID: PMC9160541.
- Chuang L-M, Soegondo S, Soewondo P, Young-Seol K, Mohamed M, Dalisay E, et al. Comparisons of the outcomes on control, type of management and complications status in early-onset and late-onset type 2 diabetes in Asia. *Diabetes Research and Clinical Practice* [Internet]. 2006 Feb;71(2):146–55. Available from: <http://dx.doi.org/10.1016/j.diabres.2005.05.007>
- Nitiyanant W, Tandhanand S, Mahtab H, Zhu XX, Pan CY, Raheja BS, et al. The Diabcare-Asia 1998 study—outcomes on control and complications in type 1 and type 2 diabetic patients. *Curr Med Res Opin.* 2002;18(5):317–27. doi: 10.1185/030079902125000822. PMID: 12240795.



**Open Access** This article is licensed under a

Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International License, which permits use, share — copy and redistribute the material in any medium or format, adapt — remix, transform, and build upon the material, as long as you give appropriate credit, provide a link to the license, and indicate if changes were made. You may do so in any reasonable manner, but not in any way that suggests the licensor endorses you or your use. You may not use the material for commercial purposes. If you remix, transform, or build upon the material, you must distribute your contributions under the same license as the original. You may not apply legal terms or technological measures that legally restrict others from doing anything the license permits. The images or other third party material in this article are included in the article's Creative Commons license, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons license and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this license, visit <https://creativecommons.org/licenses/by-nc-sa/4.0/>.