Diabetes & Metabolic Syndrome: Clinical Research & Reviews 13 (2019) 1035–1040

Contents lists available at ScienceDirect

Diabetes & Metabolic Syndrome: Clinical Research & Reviews

journal homepage: www.elsevier.com/locate/dsx

Original Article

The effects of glycemic control on morbidity and survival among diabetic patients

Mohamed Anwar Hammad*, Syed Azhar Syed Sulaiman, Usman Abubakar, Dzul Azri Mohamed Noor

Department of Clinical Pharmacy, School of Pharmaceutical Sciences, Universiti Sains Malaysia, Penang, Malaysia

ARTICLE INFO

Article history:
Received 27 December 2018
Accepted 14 January 2019

Keywords:
Controlled glycemia
Estimated 10-year survival
Glycated hemoglobin
HbA1c
Morbidity
Type 2 diabetes mellitus

ABSTRACT

Aims: The study intended to investigate the impact of controlled glycemia on morbidity and estimated 10-year survival (ES-10Y).
Methods: A cross-sectional investigation was conducted at General Penang Hospital, Malaysia. Demographic criteria and laboratory tests of patients were investigated. Controlled glycemia (CG) was recognized as glycated hemoglobin (HbA1c) $\leq$7% depending on American Diabetes Association guidelines 2018. Charlson Comorbidity Index (CCI) was used to estimate the confounding influence of co-morbidities and predict ES-10Y. Data was managed by IBM-SPSS 23.0.
Results: A total of 400 cases categorized to (44.25%) patients with CG, and (55.75%) cases had uncontrolled glycemia (UCG). HbA1c mean in CG and UCG group was (6.8 ± 0.9 vs 9.5 ± 1.6, *P*-value: 0.001). Fasting blood glucose was (7 ± 2.3 vs. 9.9 ± 4.3, *P*-value: 0.001) in CG and UCG group. CCI was (3.38 ± 2.38 vs. 4.42 ± 2.70, *P*-value: 0.001) and, ES-10Y was (62% vs 46.2%, p-value: 0.001) in CG vs. UCG respectively. Spearman test indicates a negative correlation between CG and CCI (r: 0.19, p-value: 0.001). Logistic regression confirmed HbA1c as a significant predictor of CCI (r^2: 0.036, *P*-value: 0.001). CG has a positive correlation with survival (r: 0.16, *P*-value: 0.001) and logistic regression of survival (r^2: 0.26, *P*-value: 0.001).
Conclusions: More than one-half of the investigated persons had UCG. Controlled HbA1c was associated with lower co-morbidities and higher ES-10Y.

1. Introduction

HbA_1c is a blood investigation can compute the quantity of glycated hemoglobin in the red blood cells. HbA_1c test explains what an individual's mean level of blood glucose was for the past 60–90 days before the check. HbA1c can assist in concluding how well an individual's diabetes is actuality at the target level over time. Glucose particles in the blood naturally become cemented to hemoglobin particles; this is to say that the hemoglobin has changed into glycosylated. As an individual's blood sugar becomes higher than optimal blood glucose, more of the person's hemoglobin will become glycosylated [1,2].

Type 2 diabetes is one of the furthermost serious burdens on public health regarding mortality, morbidity, and budget to the health care system [3–5]. There is a growth in the incidence of chronic diseases such as cardiovascular disease, chronic kidney diseases, dyslipidemia, diabetic eye diseases, dementia, asthma, hypertension [6–12], and obesity. This growth in comorbidities highlights the increasing worldwide liability, to evaluate the effect of HbA1c control on morbidity and estimated 10-year survival.

1.1. Research question

What is the impact of HbA1c control on co-morbidities and ES-10Y among diabetic outpatients?

2. Materials and methods

2.1. Study population

A cross-sectional study was done at Penang General Hospital, Penang, Malaysia, in the period (October 2016–2017). Diabetic

* Corresponding author. K19A, 102 - Aman Damai, Universiti Sains Malaysia, Malaysia.
E-mail addresses: m_anwaaar@hotmail.com (M.A. Hammad), sazhar@usm.my (S.A. Syed Sulaiman), pharmumma2@gmail.com (U. Abubakar), dzulazri@usm.my (D.A. Mohamed Noor).

https://doi.org/10.1016/j.dsx.2019.01.001
1871-4021/

adults with age equals or more than eighteen years were enrolled. From 400 patients, only 177 cases had controlled glycemia, and 223 patients had uncontrolled glycemia. Pregnant and type 1 diabetes patients were excluded from the analysis.

2.2. Procedure and variable assessment

A validated data collection sheet was used to collect the patients' clinical, demographics, and laboratory data from individuals, patients' medical files, and healthcare providers. Charlson Comorbidity Index (CCI) was used to estimate the confounding impact of comorbidities and predict ES-10Y of controlled and uncontrolled glycemia cohorts [13]. A diabetologist estimated patients' adherence using "*8-item Morisky medication adherence scale (MMAS-8)*". Adherence was classified as low adherence (Scores >2), medium adherence (Scores 1 or 2) and high adherence (Scores = 0) [14]. The uncontrolled glycemia was defined as (HbA1c >7% for patient <65 years, and ≥8% for patient ≥65 years) depends on American diabetes association guidelines 2018 [15]. This analysis guided by the documentation strategy for "*cross-sectional study designs and strengthening the reporting of observational studies in epidemiology (STROBE)*" [16].

2.3. Statistical analysis

The data were managed using IBM SPSS V23.0. Categorical variables were demonstrated as a number and percentage. Parametric data were explained as the mean ± standard deviation. The Kolmogorov-Smirnov test was used to evaluate the normality of the variables. Log transformation was performed on some of the skewed variables before analysis to reach a normal distribution [17]. Independent *t*-test and analysis of variance (ANOVA) estimated the differences amongst the means of continuous factors. While chi-square, Mann–Whitney U and Kruskal Wallis tests were used for evaluating the differences between the nominal and categorical variables. A confidence interval (95%) and *P*-value <0.05 were considered statistically significant. Mantel-Haenszel and analysis of covariance (ANCOVA) were used to monitor the influence of confounders. Ethical Consideration Spearman's tests and logistic regression were used to measure the strength and direction of the association between two variables.

From the ethical viewpoint, this study tracked the processes of the registration in Clinical Research Centre in Hospital Pulau Pinang and the registration in the National Medical Research Register (NMRR ID: NMRR-15-1068-25700) [18]. Every study phase was conducted under the supervision of experts and followed the tenets of the last update of the Declaration of Helsinki [19]. All contributors have signed an informed consent form. The confidentiality, dignity and data of the subjects are safe and used for the research and publication purposes only.

3. Results

About 400 cases categorized to 177 (44.25%) patients with CG, and 223 (55.75%) cases had uncontrolled glycemia (UCG). The age mean of CG and UCG was (54.8 ± 14.7) vs. (53.2 ± 14.8) years. Gender distribution was 195 (50.6%) vs. 178 (47.8%) males in CG and UCG cohort. HbA1c mean in CG and UCG group was (6.5 ± 0.66 vs 9.4 ± 1.8, *P*-value: 0.001). Fasting blood glucose was (6.9 ± 2.3 vs. 9.6 ± 4.5, *P*-value: 0.001) in CG and UCG group as described in Table 1. The regression analysis indicated that obesity, younger age of participants, poor adherence, statins therapy, and uncontrolled dyslipidemia are predictors of the uncontrolled glycemia.

CCI was (3.38 ± 2.34 vs. 4.42 ± 2.52, *P*-value: 0.001) and, estimated 10-year survival was (62% vs 46.2%, *P*-value: 0.001) in CG vs. UCG respectively. Spearman test indicates a negative correlation between CG and CCI (r: 0.19, *P*-value: 0.001) as demonstrated in Table 2. Binary logistic regression confirmed CG as a significant predictor of CCI (r^2: 0.036, *P*-value: 0.001). CG has a positive correlation with survival (r: 0.16, *P*-value: 0.001) and logistic regression of survival (r^2: 0.26, *P*-value: 0.001).

Binary logistic regression indicated that age, compliance, FBG, insulin therapy, physical activity and utilization of statins are predictors of HbA1c control among diabetic patients as shown in Table 3.

The P − P plot compares the observed cumulative distribution function of the standardized residual of to the expected cumulative function of the normal distribution of the HbA1c as described in Fig. 1.

The propensity score was done to match controlled and uncontrolled HbA1c. Propensity scale matching confirmed that statins utilization is a predictor of HbA1c control after ruling out the effects of confounders (BMI, FBG, adherence, insulin usage) as described in Table 4.

4. Discussion

Glucose control is a significant step in the management of type 2

Table 1
Variable distribution among controlled and uncontrolled HbA1c cohorts.

Variance	Controlled HbA1c n = 177 (44.25%)	Uncontrolled HbA1c n = 223 (55.75%)	P value
Age (years)	54.8 ± 14.7	53.2 ± 14.8	0.001
BMI (kg/m^2)	27.5 ± 5.8	29.1 ± 5.6	0.001
Gender:			
Male	195 (50.6%)	178 (47.8%)	0.538
Female	190 (49.4%)	194 (52.2%)	0.538
Ethnicity:			
Malay	112 (29.1%)	147 (39.5%)	0.056
Chinese	180 (46.7%)	124 (33.3%)	0.056
Indian	93 (24.2%)	101 (27.2%)	0.056
Adherence:			
Good	290 (75.3%)	160 (43%)	0.001
Poor	95 (24.7%)	212 (57%)	0.001
HbA1c(%)	6.5 ± 0.66	9.4 ± 1.8	0.001
FBG (mmol/L)	6.9 ± 2.3	9.6 ± 4.5	0.001
Charlson comorbidity index	3.38 ± 2.34	4.42 ± 2.52	0.001
Estimated 10-year survival	62%	46.2%	0.001

BMI: Body mass index, FBG: Fasting blood glucose, HbA1c: Glycated hemoglobin, (Association is significant at the P value: 0.05 level (2-tailed). Chi-square (X2) test was carried out to inspect the differences between the categorical variables. The *t*-test or Mann-Whitney *U* test, established on the skewness of data, were used for continuously distributed variables.

Table 2
The frequency of Charlson Comorbidity Index Categories of controlled glycemia group and uncontrolled glycemia cohort.

Condition	Weight	Controlled glycemia (n = 177)	CCI score (CG)	Uncontrolled glycemia (n = 223)	CCI score (UCG)
Age (years)					
50–59 years	1	32 (18.1%)	0.181	59 (26.5%)	0.265
60–69 years	2	38 (21.5%)	0.430	61 (27.4%)	0.548
70–79 years	3	27 (15.3%)	0.458	13 (5.8%)	0.174
≥80 years	4	4 (2.3%)	0.090	3 (1.3%)	0.054
Diabetes mellitus					
Uncomplicated	1	166 (93.8%)	0.938	199 (89.2%)	0.892
End-organ damage	2	11 (6.2%)	0.124	24 (10.8%)	0.215
Liver disease					
Mild	1	8 (4.5%)	0.045	23 (10.3%)	0.103
Moderate to severe	3	4 (2.3%)	0.068	10 (4.5%)	0.135
Solid Tumor					
Localized	2	4 (2.3%)	0.046	4 (1.8%)	0.036
Metastatic	6	2 (1.1%)	0.068	12 (5.4%)	0.323
AIDS	6	0 (0%)	0.000	0 (0%)	0.000
Moderate to severe CKD	2	51 (28.8%)	0.576	87 (39%)	0.780
Congestive heart failure	1	1 (0.6%)	0.006	9 (4%)	0.040
Myocardial infarction	1	20 (11.3%)	0.113	55 (24.7%)	0.247
COPD	1	2 (1.1%)	0.011	12 (5.4%)	0.054
Peripheral vascular disease	1	3 (1.7%)	0.017	2 (0.9%)	0.009
CVA or TIA	1	2 (1.1%)	0.011	7 (3.1%)	0.031
Dementia	1	17 (9.6%)	0.096	31 (13.9%)	0.139
Hemiplegia	2	2 (1.1%)	0.022	7 (3.1%)	0.062
Connective tissue disease	1	5 (2.8%)	0.028	6 (2.7%)	0.027
Leukaemia	2	1 (0.6%)	0.012	2 (0.9%)	0.018
Malignant lymphoma	2	1 (0.6%)	0.012	1 (0.4%)	0.009
Peptic ulcer disease	1	5 (2.8%)	0.028	17 (7.6%)	0.076
CCI Score (mean ± SD)			3.38 ± 2.34		4.42 ± 2.52
Estimated 10-year survival			62%		46.2%

AIDS: Acquired immune deficiency syndrome, CCI: Charlson comorbidity index, CKD: Chronic kidney diseases, COPD: Chronic obstructive pulmonary disease, CVA: Cerebrovascular accident, TIA: Transient ischemic attack.

Table 3
Binary logistic regression for HbA1c control among diabetic patients (n = 400).

		B	S.E.	Wald	df	P-value	Exp(B)
Step 1[a]	Age	0.032	0.010	10.083	1	0.001	1.033
	ACES_ARBS	−0.256	0.344	0.554	1	0.456	0.774
	BMI	−0.006	0.025	0.063	1	0.801	0.994
	Compliance	−1.600	0.269	35.255	1	0.001	0.202
	FBG	−0.251	0.066	14.563	1	0.001	0.778
	FBG_control	−0.002	0.361	0.000	1	0.995	0.998
	HTN	−0.505	0.384	1.733	1	0.188	0.603
	Insulin therapy	−1.010	0.262	14.804	1	0.001	0.364
	Physical activity	0.648	0.318	4.157	1	0.041	1.911
	Statins	1.416	0.298	22.626	1	0.001	4.122
	Constant	1.434	1.339	1.147	1	0.284	4.195

ACEIs: Angiotensin-converting enzyme inhibitors, ARBs: Angiotensin II receptor blockers, BMI: Body mass index. FBG: Fasting blood glucose, HbA1c: Glycated hemoglobin, HTN: Hypertension, (Association is significant at the P value: 0.05 level (2-tailed).
[a] Variable(s) entered on step 1 (Independent variables): Age, BMI, FBG, ACES_ARBS, Activity, Compliance, FBG_C, HTN, Insulin, Statins. (Dependent variable: HbA1c control).

diabetes mellitus. American Diabetes Association identifies HbA1c of ≤7% as the zone of well-controlled diabetes. However, the goal of HbA1c has considered <8% for patient experienced severe hypoglycemia and had microvascular or macrovascular complications (American Diabetes Association, 2018) [20]. In our study, more than fifty percent of the patients had uncontrolled glycemia, and > one-quarter of them had HbA1c >10%.

In a cross-sectional study, Alzaheb and Altemani (2018) investigated glycemic control status. They found that a high percentage of the sampled patients had inadequate glycemic control. Therefore, healthcare professionals should manage the associated risk factors to limit disease complications and improve the health of patients with diabetes [21].

Fiagbe et al. (2017) indicated that once diabetes is uncontrolled, it has horrible impacts on well-being and healthiness. Diabetes may lead to abundant extended-term problems in numerous body organs and may upsurge the total hazard of early passing. A survey that enrolled diabetic persons with age equals eighteen years and above. Data on glycemia control was mined from the patient' file. The predominance of uncontrolled glycemia was eighty-sixed percent. About six percent had controlled blood glucose level from the sixty-three patients who defaulted, as compared to about seventeen percent of the one-hundred thirty-one participants who did not default. Only fourteen percent of diabetic patients have accomplished the target of blood glucose level [22].

Rodrigo Fonseca et al. (2017) identified the factors connected with glycemia manage in diabetic persons registered in the Family Health Strategy (FHS) in Pernambuco, Brazil. Glycemia target defined as (HbA1c ≤ 7%). Around two-thirds of the patients showed uncontrolled glycemia, particularly those with younger age, more extended period of the disease, more annual communication with Family Health Strategy and complexed therapeutic schedule.

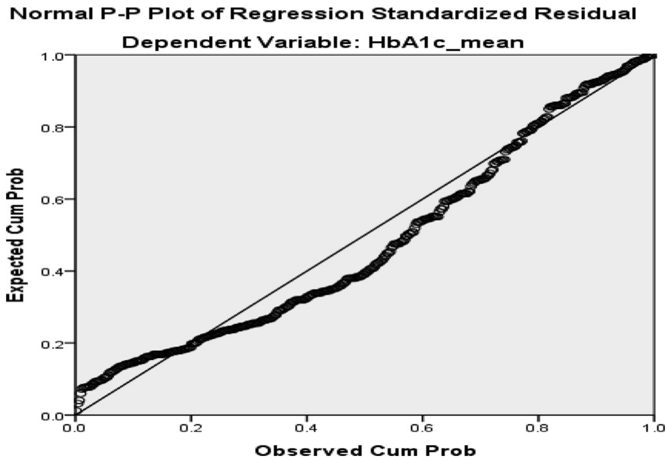

Fig. 1. Normal probability plot of HbA1c mean among diabetic patients.

Attention to diabetic youth persons and referrals to specialists are issued that can get better glycemia control [23].

In Japan, Hu et al. (2016) estimated the predominance of diabetic persons who meet HbA1c guidelines and examined the correlation of uncontrolled glycemia. The "*Japan Epidemiology Collaboration on Occupational Health (J-ECOH)*" Study planned a cross-sectional analysis of a total of 3070 diabetic workers, aged 20–69 years. Risk factor goals were defined based on both the American Diabetes Association (ADA) guidelines and the Japan Diabetes Society (JDS) guidelines (HbA1c <7.0%). A logistic regression model was conducted to evaluate correlates of inadequate glycemic control (defined as HbA1c ≥ 8.0%). The proportions of participants who met ADA and JDS goals were 44.9% for HbA1c. The poor glycemic control accompanied younger age, obesity, smoking, and uncontrolled dyslipidemia. Data from a large working population, suggest that getting off the HbA1c target was less than optimal, especially in younger participants [24].

A study by Arosemena et al. (2015) stated that a high incidence of uncontrolled diabetes at a clinic in Ecuador. Hazard factors for uncontrolled diabetes consist of age more than fifty years old and the shortage of looking for diabetes awareness. Interventions and inspire self-directed diabetes education may be targeted at patients age >50 years [25,26].

In Pakistan, a cross-sectional study by Siddiqui et al. (2015) assessed the prevalence and factors associated with, uncontrolled diabetes mellitus (UDM). The study was conducted in a community-based specialized care center (SCC) for diabetes. About 452 with type 2 DM subjects were tested for HbA1c. Prevalence of UDM among diabetes patients was found to be 38.9% (95% CI: 34.4–43.4%). Multivariable logistic regression model analysis indicated that UDM was independently associated with age <50 years (OR: 1.9; 95% CI: 1.2–2.9). Also, if they were diagnosed in a hospital, (vs. a clinic) (OR: 1.8; 95% CI: 1.1–2.8), diabetes data from a doctor or nurse only (vs. multiple sources) (OR: 1.8; 95% CI: 1.2–2.9). Alternatively, in case higher monthly therapy cost (OR: 1.3; 95% CI: 1.1–1.6; for every extra 500 PKR), and higher intake of tea (OR: 1.5; 95% CI: 1.0–2.2; for every two additional cups). The prevalence of UDM was about 39% among persons with type 2 diabetes visiting SCC for diabetes. Adaptable hazard issues such as sources of diabetes data and tea ingestion can be considered as likely targets of interventions [27].

In this study, Charlson comorbidity index score of the cohort with controlled glycemia is lower than the group of uncontrolled glycemia. The estimated 10-year survival among controlled glycemia group is higher than the cohort of uncontrolled glycemia.

A retrospective cohort study by Pantalone et al. (2018) assessed the longitudinal accumulation of diabetes-related complications and the impact of glycemic control on the Diabetes Complications Severity Index (DCSI) score in people with type 2 diabetes. Individuals with newly diagnosed type 2 diabetes (NDT2D) were recognized between 2005 and 2016 and classified by baseline HbA1c category (<7%, <8%, ≥8%). The DCSI scores were estimated for each study year, and the snowballing occurrence of diabetic complications was determined. Of 32 174 people identified as having NDT2D, 14 016 (44%) had an initial HbA1c <7%, 21 657 (67%), had a baseline HbA1c <8%, and 9983 (31%) had HbA1c ≥ 8%. After ten years of diabetes diagnosis, chronic kidney disease was diagnosed in 22%, coronary heart disease 29%, neuropathy 24%and retinopathy 36% of patients. Initial glycated hemoglobin did not affect the observed trend in longitudinal changes in DCSI scores throughout the 11 years. For persons in each of the baseline HbA1c cohorts (<7%, <8%, ≥8%) persistently inadequate glycemic control was significantly concomitant with a 10%, 19%, or 16% increase in the risk of experiencing an augmented DCSI score, respectively (all *P-value* < 0.01). Persistently or worsening poor glycemic control was concomitant with an increased risk of a rise in the DCSI score [28].

Ikeda et al. (2017) clarified the connection amongst cardiac systolic/diastolic function, heart failure (HF) prognosis, and HbA1c throughout guideline-directed medical treatment in patients with "*non-ischemic dilated cardiomyopathy (NIDCM)*". They assessed 283 hospitalized NIDCM persons, who were clustered regarding baseline (BL) and 1-year (1Y) levels of HbA1c (<6.0, 6.0–6.9, and ≥7.0%). The main endpoint was recognized as either cardiac death or readmission for HF worsening. Almost 50% of the subjects had baseline- or 1Year-HbA1c ≥ 6.0% (31% at baseline, 34% at 1year had 6.0–6.9%; 12% at baseline, 12% at 1year had ≥7.0%). The value of the left ventricular (LV) ejection fraction and its development throughout one year showed no significant variance among the 1Year-HbA1c associates (*P-value*: 0.273). A further noteworthy decrease in the prompt diastolic speed of the mitral annulus (Ea) was seen in the group with 1Y-HbA1c ≥ 7.0% (both *P-value* < 0.001). In multiple regression examinations, lesser 1Y-Ea and higher 1Y-plasma B-type natriuretic peptide were independently related with higher 1Y-HbA1c (both adjusted *P-value* < 0.05). The snowballing

Table 4
Propensity score matching of controlled and uncontrolled HbA1c among diabetic patients.

Predictive variable		B	S.E.	Wald	df	P value	Exp(B)
Step 1[a]	BMI	−0.046	0.022	4.313	1	0.038	0.955
	FBG	−0.248	0.064	14.981	1	0.001	0.780
	Physical Activity	0.537	0.309	3.025	1	0.082	1.711
	Compliance	−1.644	0.263	39.166	1	0.001	0.193
	FBG Control	−0.035	0.355	0.010	1	0.921	0.965
	Insulin	−0.938	0.255	13.526	1	0.001	0.391
	Statins	1.253	0.264	22.439	1	0.001	3.500
	Constant	4.130	0.923	20.035	1	0.001	62.204

[a] Variable(s) entered on step 1: BMI, FBG, Physical Activity, Compliance, FBG Control, Insulin, Statins. BMI: Body mass index, FBG: Fasting blood glucose.

occurrence of the chief endpoint was uppermost in the group with 1Y-HbA1c $\geq$ 7.0% (log-rank *P-value*: 0.001). Multivariate investigation showed that higher 1Y-HbA1c was individualistically connected with a higher occurrence of the primary endpoint (adjusted *P-value*: 0.005). They concluded that uncontrolled glycemia throughout clinical tracking-up is a hazard feature for the development of concomitant LV irregular relaxation, resulting in poor HF prediction in patients with NIDCM [29].

Low Wang et al. (2016) stated that there is plentiful epidemiological data support the association between hyperglycemia and increased cardiovascular risk. Sarwar et al. (2010) stated there is strong evidence indicating a higher risk for ASCVD with increasing dysglycemia, with an estimated 11%–16% rise in cardiovascular diseases (CVD) for every 1% increase in HbA1c [30]. Eeg-Olofsson et al. (2010) stated that the Swedish National Diabetes Register provided compelling evidence for HbA1c as a predictor of nonfatal and fatal coronary heart disease (CHD), nonfatal and fatal stroke, nonfatal and fatal CVD, fatal CVD, and total mortality. They conducted a study of 18334 persons with type 2 diabetes followed over an average of 5.6 years [31]. The relationship between HbA1c and the macrovascular disease appears linear and is observed in patients with shorter ($\leq$7 years) and a longer period of diabetes, previous history of CVD, and different types of glycemic therapy. Also, a 12% increase in ASCVD risk for every 18 mg/dL (1 mmol/L) increase in fasting glucose >105 mg/dL. A similar 13% increased hazard ratio for vascular-death for every 18-mg/dL rise in FSG >100 mg/dL (5.6 mmol/L) was verified by the Emerging Risk Factors Collaboration group. There are comparable findings in numerous studies [32].

Controlled HbA1c and blood glucose levels are suggested in the literature on the diabetes management. Arnold and Wang (2014) examined the association between all-cause mortality and HbA1cby a meta-analysis of observational revisions. An extensive examination of the literature was piloted. About seven qualified observational revisions were elaborated in the study. A noteworthy J-shaped association was detected amid all-cause mortality and HbA1c. This augmented mortality at high and low HbA1c targets has significant magnitudes on considering optimal clinical HbA1c targets as it designated that there are inferior and superior restrictions for generating a 'security zone' (6–8%) for managing of diabetes [33].

In a systematic review and meta-analysis, Cavero-Redondo et al. (2017) examined the association among the risk of cardiovascular (CV) outcomes, all-cause mortality and level of glycated hemoglobin based on statistics from observational revisions, and to determine the optimal levels of HbA1c for avoidance CV events and/or death in diabetic patients. They systematically searched electronic databases, from inception to 2016, for studies addressing the association of HbA1c levels with mortality and CV outcomes. Random effects models were conducted to determine combined evaluations of risk ratio and corresponding 95% confidence interval for risk of CV events, CV mortality, and all-cause mortality independently for persons plus and minus diabetes. Only forty-six studies could be incorporated in the meta-analysis. In diabetic populations, there was an increase in the risk of all-cause mortality when HbA1c levels were over eight percent and below six percent. Their findings establish optimal HbA1c levels, for the lowest all-cause and CV mortality, fluctuating from six percent to eight percent in diabetic people [34].

5. Conclusion

Nearly more than fifty percent of the studied patients had uncontrolled glycemia. Controlled HbA1c was associated with lower co-morbidities and higher estimated 10-year survival.

Interest conflicts

The authors have no inconsistency of interest to declare.

Conflicts of interest

All the authors do not have any possible conflicts of interest.

Authors' contributions

- MAH contributed in the conception of the work, data collection, data analysis, manuscript drafting, manuscript revising, and approval of manuscript final, all aspects of the work and agreed for all aspects of the work.
- UA contributed in the conception of the work, manuscript drafting, manuscript revising, manuscript final approval and agreed for all aspects of the work
- SASS contributed in the conception of the work, manuscript drafting, manuscript revising, and manuscript final approval and agreed for all aspects of the work.
- DAMN contributed in the conception of the work, data analysis, manuscript drafting, manuscript revising, and approval of manuscript final and agreed for all aspects of the work.

The manuscript has been read and approved by all the authors, that the requirements for authorship as stated earlier in this document have been met, and that each author believes that the manuscript represents honest work.

Funding support and sponsorship

Universiti Sains Malaysia supported this research (USM Fellowship 4/15).

Acknowledgment

The authors are appreciative to all of the staff at the department of endocrine, department of pharmacy and laboratory teams in Hospital Pulau Pinang for their kind help and support in facilitating this study. Special appreciations to Universiti Sains Malaysia for financially supporting this research.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.dsx.2019.01.001.

References

[1] Hemoglobin A1c (HbA1c) test for diabetes. Diabetes guide. Retrieved 21 March 2018 from https://www.webmd.com/diabetes/guide/glycated-hemoglobin-test-hba1c.

[2] Sherwani SI, Khan HA, Ekhzaimy A, Masood A, Sakharkar MK. Significance of HbA1c test in diagnosis and prognosis of diabetic patients. Biomark Insights 2016;11:95–104. https://doi.org/10.4137/BMI.S38440.

[3] Hammad MA, Tangiisuran B, Kharshid AM, Abdul-Aziz N, Hassan Y, Aziz NA, et al. Drug-drug interaction-related uncontrolled glycemia. J Pharm Bioall Sci 2017;9:221–8.

[4] Hammad MA, Khamis AA, Al- Akhali KM, Elsayed TM, Alasmri AM, Al-Ahmari EM, et al. Evaluation of drug dosing in renal failure. IOSR-JPBS 2016;11(5):39–50. https://doi.org/10.9790/3008-1105033950. 3.

[5] Hammad MA, Mohamed Noor DA, Syed Sulaiman SA. The effect of patients' adherence on HbA1c control. AMPSR 2017;1(1):30–5.

[6] Hammad MA, Alakhali KM, Hattan M, Mohamed Noor DA, Syed Sulaiman SA, Kharshid AM, et al. Asthma in Saudi arabia: risk factors and pharmacotherapy. IAJPR 2016;6(11):6814–21. https://doi.org/10.1044/1980-iajpr.161043.

[7] Alakhali KM, Ansari MA, Hammad MA. Analysis of prevalence, risk Factor and pharmacotherapy of hypertension in outpatients. IJOPP 2013;4(6):64–6.

[8] Hammad MA, Mohamed Noor DA, Syed Sulaiman SA, Khamis AA, Kharshid A, Aziz NA. Comparison of statins dose intensity on HbA1c control in outpatients

with type 2 diabetes: a prospective cohort study. International Journal of Pharmacological and Pharmaceutical Sciences 2017;11(8):466–71.

[9] Al Akhali K, Hammad MA, Ansari MA. Evaluation of prevalence and pattern of anemia – a hospital based study in aseer province, Kingdom of Saudi Arabia. Journal of Experimental Medical & Surgical Research 2013;2:32–5.

[10] Hammad MA, Mohamed Noor DA, Syed Sulaiman SA, Elsayed TM. Statins effects on diabetic retinopathy among patients with type 2 diabetes mellitus. International Journal of Ophthalmology & Visual Science 2017;2(4):106–14. https://doi.org/10.11648/j.ijovs.20170204.15.

[11] Hammad MA, Syed Sulaiman SA, Aly A, Mohamed Noor DA. Malaysian adaptation of the mini-addenbrooke's cognitive examination (M-ACE). WASJ 2017;35(11):2315–20. https://doi.org/10.5829/idosi.wasj.2017.2315.2320.

[12] Alakhali KM, Selim M, Hammad MA. Evaluation of therapeutic drug monitoring of cyclosporine and tacrolimus in kidney transplant patients. JPCS 2014;8:18–25.

[13] Chang CM, Yin WY, Wei CK, Wu CC, Su YC, Yu CH, et al. Adjusted age-adjusted Charlson Comorbidity Index score as a risk measure of perioperative mortality before cancer surgery. Palaniyandi S PLoS One 2016;11(2), e0148076. https://doi.org/10.1371/journal.pone.0148076.

[14] Janežič A, Locatelli I, Kos M. Criterion validity of 8-item Morisky Medication Adherence scale in patients with asthma. Leroyer C PLoS One 2017;12(11), e0187835. https://doi.org/10.1371/journal.pone.0187835.

[15] American Diabetes Association. Older adults, standards of medical care in diabetes—2018. Diabetes Care 2018;41(Suppl. 1):S1–2. https://doi.org/10.2337/dc18-SINT01.

[16] STROBE statement. STROBE checklists. Checklist for cross-sectional studies 2017. Retrieved 21 March 2018 from: https://www.strobe-statement.org/index.php?id=available-checklists.

[17] Mazoochian L, Mohammad Sadeghi HM, Pourfarzam M. The effect of FADS2 gene rs174583 polymorphism on desaturase activities, fatty acid profile, insulin resistance, biochemical indices, and incidence of type 2 diabetes. J Res Med Sci 2018;23:47.

[18] National Medical Research Register, National Institute of Health NIH guideline. Retrieved 31 March 2018 from: https://www.nmrr.gov.my/fwbLoginPage.jsp?fwbPageId=NMRR_Home.

[19] World Medical Association. World medical association declaration of Helsinki ethical principles for medical research involving human subjects. J Am Med Assoc 2013;310(20):2191–4. https://doi.org/10.1001/jama.2013.281053.

[20] American Diabetes Association. Standards of medical care in diabetes-2018. Diabetes Care 2018;41(Suppl. 1):S55–64. https://doi.org/10.2337/dc18-Sint01.

[21] Alzaheb RA, Altemani AH. The prevalence and determinants of poor glycemic control among adults with type 2 diabetes mellitus in Saudi Arabia. Diabetes Metab Syndr Obes 2018;11:15–21. https://doi.org/10.2147/DMSO.S156214.

[22] Fiagbe J, Bosoka S, Opong J, Takramah W, Axame WK, Owusu R. Prevalence of controlled and uncontrolled diabetes mellitus and associated factors of controlled diabetes among diabetic adults in the hohoe municipality of Ghana. Diabetes Manag 2017;7(5):343–54.

[23] Lima RF, Fontbonne A, Carvalho EMF, Montarroyos UR, Barreto MNSC, Cesse EÂP. Factors associated with glycemic control in people with diabetes at the Family Health Strategy in Pernambuco. Rev Esc Enferm USP 2016;50(6):937–45. https://dx.doi.org/10.1590/s0080-623420160000700009.

[24] Hu H, Hori A, Nishiura C, Sasaki N, Okazaki H, Nakagawa T, et al. HbA1c, blood pressure, and lipid control in people with diabetes: Japan Epidemiology Collaboration on Occupational Health Study. PLoS One 2016;11(7):1–13. e0159071, http://doi.org/10.1371/journal.pone.0159071.

[25] Arosemena CM, Sánchez AJ, Tettamanti MD, Vasquez CD, Chang A, Navarro CM. Prevalence and risk factors of poorly controlled diabetes mellitus in a clinical setting in Guayaquil, Ecuador: a Cross-Sectional Study. Int J Diabetes Clin Res 2015;2(4):1–5.

[26] Nicholas J, Charlton J, Dregan A, Gulliford MC. Recent HbA1c values and mortality risk in type 2 diabetes. population-based case-control study. Berthold HK PLoS One 2013;8(7), e68008. https://doi.org/10.1371/journal.pone.0068008.

[27] Siddiqui FJ, Avan BI, Mahmud S, Nanan DJ, Jabbar A, Assam PN. Uncontrolled diabetes mellitus: prevalence and risk factors among people with type 2 diabetes mellitus in an Urban District of Karachi, Pakistan. Diabetes Res Clin Pract 2015;107(1):148–56. https://doi.org/10.1016/j.diabres.2014.09.025.

[28] Pantalone KM, Misra-Hebert AD, Hobbs TM, Wells BJ, Kong SX, Chagin K. Effect of glycemic control on the Diabetes Complications Severity Index score and development of complications in people with newly diagnosed type 2 diabetes. J Diabetes 2018;10(3):192–9. https://doi.org/10.1111/1753-0407.12613.

[29] Ikeda Y, Inomata T, Fujita T, Iida Y, Kaida T, Nabeta T. Higher hemoglobin A1c levels are associated with impaired left ventricular diastolic function and higher incidence of adverse cardiac events in patients with nonischemic dilated cardiomyopathy. Heart Ves 2017;32(4):446–57. https://doi.org/10.1007/s00380-016-0895-x.

[30] Sarwar N, Gao P, Seshasai SR, Gobin R, Kaptoge S, Di AE. Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative meta-analysis of 102 prospective studies. Lancet 2010;375:2215–22.

[31] Eeg-Olofsson K, Cederholm J, Nilsson PM, Zethelius B, Svensson AM, Gudbjörnsdóttir S, et al. New aspects of HbA1c as a risk factor for cardiovascular diseases in type 2 diabetes: an observational study from the Swedish National Diabetes Register (NDR). J Intern Med 2010;268:471–82. https://doi.org/10.1111/j.1365-2796.2010.02265.x.

[32] Low Wang CC, Hess CN, Hiatt WR, Goldfine AB. Clinical update: cardiovascular disease in diabetes mellitus atherosclerotic cardiovascular disease and heart failure in type 2 diabetes mellitus – mechanisms, management, and clinical considerations. Circulation 2016;133:2459–502. https://doi.org/10.1161/CIRCULATIONAHA.116.022194.

[33] Arnold LW, Wang Z. The HbA1c and all-cause mortality relationship in patients with type 2 diabetes is J-shaped: a meta-analysis of observational studies. Rev Diabet Stud 2014;11(2):138–52. http://doi.org/10.1900/RDS.2014.11.138.

[34] Cavero-Redondo I, Peleteiro B, Álvarez-Bueno C, Rodriguez-Artalejo F, Martínez-Vizcaíno V. Glycated haemoglobin A1c as a risk factor of cardiovascular outcomes and all-cause mortality in diabetic and non-diabetic populations: a systematic review and meta-analysis. BMJ Open 2017;2017(7), e015949. http://doi.org/10.1136/bmjopen-2017-015949.