



A report of two cases of type 2 diabetes mellitus (T2DM): happy and longevity

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ABSTRACT

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Chronic hyperglycemia in patients with type 2 diabetes mellitus (T2DM) is associated with the development of complications and the increase of risk of mortality. Patients with T2DM have a shorter life expectancy than non-diabetic population. It is attributed to cardiovascular disease, stroke, renal disease, and infection. Depression secondary to T2DM worsens the quality of life. On the contrary, positive emotions correlated strongly with long life expectancy. A number of mechanisms might explain this correlation. We reported two geriatric patients over 80 y.o. with T2DM comorbidity for more than 20 years. Discussion point of these cases is the subject's longer life span compared to the average diabetic patient's life expectancy and great quality of life despite the disease burden of chronic hyperglycemia in T2DM and cardiovascular risk.

ABSTRAK

Hiperglikemia kronis pada pasien diabetes mellitus tipe 2 (DMT2) dikaitkan dengan perkembangan komplikasi dan peningkatan risiko kematian. Pasien diabetes memiliki harapan hidup yang lebih pendek daripada populasi non-diabetes. Hal ini dikaitkan dengan penyakit kardiovaskular, stroke, penyakit ginjal, dan infeksi. Depresi sekunder akibat DMT2 memperburuk kualitas hidup. Sebaliknya, emosi positif berhubungan kuat dengan harapan hidup yang panjang. Sejumlah mekanisme mungkin menjelaskan hubungan ini. Kami melaporkan dua pasien geriatri berusia di atas 80 tahun dengan komorbiditas DMT2 selama lebih dari 20 tahun. Poko diskusi dari kasus ini adalah rentang hidup subjek yang lebih lama dibandingkan dengan rerata harapan hidup pasien diabetes dan kualitas hidup yang baik meskipun mempunyai beban penyakit hiperglikemia kronis pada DMT2 dan risiko penyakit kardiovaskular.

Keywords:

chronic hyperglycemia;
type 2 diabetes;
life expectancy;
life quality;
risk factor

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a group of metabolic disease characterized by hyperglycemia that results from inadequate insulin secretion or defects in tissue response to insulin.¹ Untreated hyperglycemia in uncontrolled DM over time leads to various organ damage and dysfunctions.^{2,3} Type 2 diabetes mellitus is a significant risk factor for cardiovascular disease, chronic kidney disease, peripheral nerve disease and,

other complications.^{4,5} Diabetes mellitus is associated with increased risk for mortality and morbidity in both men and women, especially from cardiovascular disease, in which nearly half of the cases are due to stroke. Mortality in T2DM adult patients is twice higher compared to adults without T2DM.^{6,7}

Psychosocial factors such as disease burden, interpersonal relationships, social supports, and emotional disturbances contributes to quality of life in T2DM patients.⁸ Constant behavior of

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diabetes self-care which revolves around medication adherence, blood glucose monitoring, diet intake, eating patterns, physical activity and prevention of disease progression are reported to be directly associated with DM-related distress.^{9,10}

Emotional well-being is an important part of diabetes care and self-management. Integrating mental and physical health care can improve quality of life outcomes.^{11,9} Happier people tend to maintain better physical health and longer life expectancy. Mortality risk is lower in happier adults than less happier adults and happiness may be associated with overall better health outcomes and longevity.^{12,13}

Subjects in our cases are diabetic patients who exceeded the average of diabetic patient's life expectancy. Both subjects were diagnosed with T2DM for over 20 years, aged more than 80 y.o. and live normally. The subjects presented with uncontrolled high blood glucose level to achieve expected HbA1C target level. The patients were not distressed despite the emotional response of having been diagnosed with T2DM and carried out daily activities contently.

CASE 1

Mrs. SA, an 84 y.o woman diagnosed with T2DM in May 2000, was born on January 11, 1937. She was prescribed glibenclamide and metformin for three years. She did not comply with routine self-monitoring of blood glucose and on visits to the outpatient diabetes clinic even though her blood glucose level was always above 200 mg/dL. HbA1C level on this patient was not regularly evaluated due to lack of routine hospital visits. The patient obtained her medicine through her private provider. Patient's body weight ranges from 58 to 55 kg and her height is 150 cm. She put no limitations or restrictions to her diet and the amount of food that she included in her diet was sufficient. Her occupation

is a college lecturer which serves as her daily physical activity.

She reported symptoms of cephalgia and her blood glucose level was over 300 mg/dL upon testing in May 2000. Glibenclamide and metformin prescription was permanently discontinued, substituted with insulin until recently and her blood glucose level improved, approaching 200 mg/dL on routine testing.

The patient was admitted to hospital in June 2016 due to severe hyperglycemia which was provoked by insulin injection noncompliance for 7 days prior to hospitalization. The patient was diagnosed with stroke due to slight paralysis in her right extremities on examination finding. Treatment for her neurological deficit lasted for a few months and the patient was able to recover completely with slight speech impairment sequelae. The patient was also prescribed amlodipine 5 mg on account of high blood pressure and later the blood pressure was successfully lowered.

The patient's visual acuity was normal and was not aided with glasses for daily activities. Complain of tingling sensation on her toes was recorded and her caregiver prescribed mecobalamin which effectively reduced the symptoms. Her sleep schedule is quite stable, which requires her to go to bed at 10 PM and then rise at 3 AM to conduct routine prayer. She always exudes a positive energy personality and is always kept company by family and friends.

The patient's recent treatment regimen includes insulin mix 30/70 with 14 unit doses on every meal and mecobalamin 500µg taken once a day. The patient's weight is 56 kg, height 155 cm and blood pressure is 120/70 mmHg.

Laboratory result

Laboratory results in 2020 and 2021 are presented in TABLE 1.

TABLE 1. Laboratory result of general check up

Components	Result per May 4 th , 2020	Result per April 21 st , 2021
HbA1 (%)	8.6	10.5
BUN (mg/dL)	25.3	34
Creatinine (mg/dL)	1.24	1.27
Cholesterol (mg/dL)	272	271
HDL-C (mg/dL)	52	45
LDL_C (mg/dL)	161	173
Triglyceride (mg/dL)	297	267

Geriatric depression Scale on May 18th, 2021

Total score of Geriatric Depression Scale on May 18th 2021, was 3. The score was obtained after ask question YES or NO answer from the following list of questions 1) Are you basically satisfied with your life? **YES/NO**; 2) Have you dropped many of your activities and interests? **YES/NO**; 3) Do you feel that your life is empty? **YES/NO**; 4) Do you often get bored? **YES/NO**; 5). Are you in good spirits most of the time? **YES/NO**; 6). Are you afraid that something bad is going to happen to you? **YES/ NO**; 7). Do you feel happy most of the time? **YES/ NO**; 8). Do you often feel helpless? **YES/ NO**; 9). Do you prefer to stay at home, rather than going out and doing new things? **YES/NO**; 10). Do you feel you have more problems with memory than most? **YES/NO**; 11). Do you think it is wonderful to be alive now? **YES/NO**; 12). Do you feel pretty worthless the way you are now? **YES/NO**; 13). Do you feel full of energy? **YES/NO**; 14). Do you feel that your situation is hopeless? **YES/NO**; 15). Do you think that most people are better off than you are? **YES/NO**.

CASE 2

Mrs. SD, an 81 y.o. woman born on May 10th, 1940, was diagnosed with T2DM

in 1998. At the time of initial diagnosis, the patient had an ulcer in her feet that resisted for more than a month with a blood glucose level of 400 mg/dL. She possessed familial risk of T2DM as her sister was also diagnosed with T2DM. She was prescribed glibenclamide and metformin. The patient's blood glucose level was recorded over 200 mg/dL multiple times. She visited her doctor regularly once a month, but HbA1C level was not regularly evaluated. The patient did not limit her food consumption and did not do the recommended physical exercise, such as jogging and aerobic exercise. Her daily recorded activities include walking during work.

The patient's treatment regimen was changed to insulin therapy in 2001 because the patient's body weight decreased, and her blood glucose did not achieve targeted level. Her body weight was recorded 37 kg and her height was 148 cm. After being treated with insulin her body weight increased by 8 kg to 45 kg. She still included refined sugar and processed foods in her diets, hence the >200 mg/dL blood glucose level customarily.

The patient also had dyslipidemia and was treated with simvastatin. The treatment was discontinued after her cholesterol level decreased to normal cut-off. She had hypertension simultaneously with her initial diagnosis with T2DM

and was prescribed amlodipine 5 mg routinely.

In 2019, the patient was diagnosed with peripheral arterial disease upon presenting with symptoms of intermittent claudication and the result of ankle brachial index examination was <0.9 thus the doctor prescribed her clopidogrel 75 mg routinely. She also complained of blurred vision on her right eye and was diagnosed with cataract, yet she objected to undergo surgery and visual acuity in her left eye was not impaired.

She lived with her sons, grandchildren and she had a happy family. Sometimes her pupils visited her house as she was their former lecturer and they had missed her. Lately she started light physical activity by walking

in the morning for approximately 500 m. She conducted religious practices every day and had a good quality of life with her family.

The patient’s treatment regimen consisted of insulin mix aspart/glargine 50/50 14 unit doses on every meal, amlodipine 5mg once a day, CPG 75mg once a day, folic acid 1mg once a day and mecobalamin 500µg once a day. The patient’s body weight is 46 kg, height is 145 cm, and blood pressure 130/80 mmHg.

Laboratory result

Laboratory results showed numbers of following components are presented in TABLE 2.

TABLE 2. Laboratory result of general check up

Components	Result per January 9th, 2020	Result per March 18st, 2021
FBG (mg/dL)	180	243
BUN (mg/dL)	-	16.9
Creatinine (mg/dL)	1.25	0.67
Uric acid (mg/dL)	7.3	4.9
Triglyceride (mg/dL)	135	171
Cholesterol (mg/dL)	-	239
LDL_C (mg/dL)	120	143

Geriatric depression scale on May 19th, 2021

Total score of Geriatric Depression Scale on May 19th, 2021 was 2. The score was obtained after ask question YES or NO answer from the following list of questions as performed in Case 1 1). Are you basically satisfied with your life? **YES/NO**; 2). Have you dropped many of your activities and interests? **YES/NO**; 3). Do you feel that your life is empty? **YES/NO**; 4). Do you often get bored? **YES/NO**; 5). Are you in good spirits most of

the time? **YES/NO**; 6). Are you afraid that something bad is going to happen to you? **YES/NO**; 7). Do you feel happy most of the time? **YES/NO**; (8). Do you often feel helpless? **YES/NO**; 9). Do you prefer to stay at home, rather than going out and doing new things? **YES/NO**; 10). Do you feel you have more problems with memory than most? **YES/NO**; 11). Do you think it is wonderful to be alive now? **YES/NO**; 12). Do you feel pretty worthless the way you are now? **YES/NO**; 13). Do you feel full of energy? **YES/NO**; 14). Do you feel that your situation is

hopeless? YES/NO; 5). Do you think that most people are better off than you are? YES/NO.

DISCUSSION

Previous study conducted in 2012 reported that 43% T2DM-related mortality occurs before the age of 70 y.o.¹ The study estimated T2DM patients' life expectancy decreases with age because organ dysfunction complication risk allows diabetic patients to have significantly lower health-related quality of life.¹⁴⁻¹⁸

Shorter life expectancy in diabetic population is largely attributed to cardiovascular complications. Patients with poor glucometabolic control are posed to 4-fold higher risk of dying from ischemic heart disease compared to non-diabetic population.^{19,20} Life expectancy predictors for T2DM patients specifically attributed to cardiovascular risks are age, sex, body mass index (BMI), systolic blood pressure, HbA1C level, total:HDL cholesterol ratio, and smoking status. If all the combined risk factors are successfully reduced, life expectancy would increase.²¹

The study resulted in significant decrease of mortality after the age of 60 y.o. in diabetic population related to comorbidities and complications factor.²² Mean age of death was significantly higher in women compared to men in diabetic population.²³ The 2019 World Health Organization's life expectancy reported the fact that men had a shorter life span than women which can be attributed to ischemic heart disease, traffic injuries, lung cancer, chronic obstructive pulmonary disease, and stroke.²⁴ In this case, the subject is an 80 y.o. diabetic female with T2DM for over 20 years. Tachkov *et al.*²² reported a progressive increase in life expectancy and reduction in mortality in female diabetic population.

Patients with T2DM and elevated

HbA1c levels of $\geq 6.5\%$ are exposed to increasing microvascular and macrovascular complication and are associated with unfavorable outcomes.^{3,25} Chronic or intermittent hyperglycemia activates diacylglycerol formation, protein kinase C, NADPH-oxidase, the production of reactive oxygen species (ROS), and oxidative stress. These inflammatory reactions are mediated by a pathological cellular death and may be aggravated by the action of advanced glycation end products, an interaction with the respective receptor for advanced glycation end products. These process leads to chronic low-grade inflammation that is mechanism of diabetes complications.²⁶ Achieving HbA1C targets of $<7\%$ are associated with reduced onset or progression of some microvascular complications lead to significantly decreased risk of macrovascular and death.²⁷ The subject in this study was presenting with neuropathy, retinopathy and PAD symptoms, but their quality of life and daily activities were not impaired. Blood glucose level and HbA1C level in these patients were not routinely controlled. The Case 1 HbA1C level recorded in May 2020 was 8.6% and in the Case 2 blood glucose levels were recorded for more than 200 mg/dL multiple times.

Other symptoms such as hypertension and dyslipidemia often coexist with T2DM as metabolic diseases add the risk factors for atherosclerotic cardiovascular disease. Some studies reported that $<140/90$ mmHg blood pressure reduces cardiovascular events as well as microvascular complications.²⁸⁻³¹ A meta-analysis showed that lowering LDL cholesterol possess beneficial effects on atherosclerotic cardiovascular disease outcomes and further persistent statin regimens reduced the incidence of these major vascular events.³² The both subjects had hypertension and were prescribed amlodipine routinely hence the blood pressure steadiness. The

patients also had dyslipidemia but were not routinely treated with statin. These two patients have low cardiovascular risks based on the study conducted by Hedayatnia *et al.*³³ After adjusting for confounding factors (age, BMI, family history of cardiovascular disease, smoking status (non-smoker, ex-smoker and current smoker), lipid lowering drug treatment, antihypertensive drug treatment, hypertension, healthy eating index, total energy intake, and presence of DM, Hedayatnia *et al.*³³ reported that only triglyceride baseline level is significantly associated with the risk of infarct myocard on male patient but not on female patient.

The other significant cardiovascular predictor presented by our patients were BMI because both of the patients did not partake in smoking. Obesity is associated with abnormal endothelial function which decreased in nitric oxide level. It may be related to elevated oxidative stress or may result from proinflammatory cytokines. Decrease in the function of nitric oxide would result in vasoconstriction and increase in vascular resistance that may predispose to cardio vascular disease risk factors.³⁴ Obesity management had been proven beneficial in treatment of morbidly obese patients with T2DM along with modest and sustained weight loss to improve glycemic control and reducing medications needed to lower high blood glucose level.^{34,35} The second subject's BMI was normal and the first subject's BMI was between 25.8 – 24.4 kg/m², interpreted as overweight and stage 1 obesity in Asian population. The first case maintained a normal BMI throughout her T2DM therapy, and the second case underwent weight increasing despite being in normal range.

The other factor attributing to improved outcome in T2DM patients is psychosocial factors namely social and emotional.^{12,13} Happier people tend to have overall better physical health and

longer survival. Happiness appears to be inversely related to perceived stress and may protect against illness through better immune response. An important indicator of overall happiness are people's cognitive and affective evaluations of their lives has been robustly linked to better physical health.³⁶⁻³⁸ In these cases, the subjects are supported by accepting families and people with positive thoughts. The first case obtained a low geriatric depression scale as well as a second case.

Happiness as an emotion formed as a general interaction between internal and external factors. Biological factors as endogenic factors are significant predictors of happiness. Genetic, brain, neurotransmitters, endocrinology, hormones, physical health, morphology, and physical attractiveness are endogenic factors that influence happiness. Neurotransmitters are Dopamine, Serotonin, Norepinefrine, and Endorphin play a role in control of happiness.^{38,39}

Studies indicate that up to 50% of the variance in happiness between individuals can be attributed to genetic influences.³⁷ There are two genes investigated directly on happiness: 5-HTTLPR and MAO-A. The 5-HTTLPR gene is coding serotonin distribution in brain cells and therefore leads to mood regulation. There are two different functional forms for this gene: Long one (L), Short one (S). Genetic factors significantly influence individual subjective well-being or happiness. A particular genotype— 5-HTTLPR 'long'—is identified as having a sizable positive association with self-reported life satisfaction. The long polymorphism thus results in increased gene expression and more serotonin transporters in the cell membrane. Individuals with long 5-HTTLPR alleles display a significant bias toward processing positive information and selectively avoiding negative information.⁴⁰

Serotonin is a neurotransmitter that mediates satisfaction, happiness, and optimism. Serotonin levels decreased in depression, and increased serotonin level is related to positive mood.⁴¹⁻⁴⁴ Most serotonin is distributed outside of the central nervous system and influences a wide range of physiologic processes in many organs. Serotonin present in CNS is only 2% and plays a pivotal role in the etiology of many mental disorders. The serotonin receptors are expressed outside as well as within the brain. Serotonin regulates numerous biological processes including cardiovascular function, bowel motility, ejaculatory latency, and bladder control and regulate some processes, including platelet aggregation by receptor-independent, secretion of cytokines, transglutaminase-dependent covalent linkage to cellular proteins.⁴⁵⁻⁴⁹

This study did not cover internal contributing factors, genetic factors, and neurotransmitters that influence happiness and mood. The authors find it interesting to identify multifaceted factors that are associated with T2DM and longevity. Unveiling factors that influence the longevity in T2DM will improve the understanding of underlying biological processes in T2DM patients.

CONCLUSION

We reported two geriatric patients over 80 y.o. with T2DM comorbidity for more than 20 years. Discussion point of these cases is the subject's longer life span compared to the average diabetic patient's life expectancy and great quality of life despite the disease burden of chronic hyperglycemia in T2DM and cardiovascular risk. It is an appealing point of interest to conduct future research to study the relationship between T2DM and longevity risk factors.

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