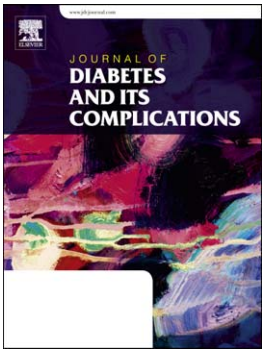

The fasting serum triglyceride levels of elderly population with different progression stages of diabetes mellitus in China

Yi-Xiong Gao, Qingqing Man, Shanshan Jia, Yuqian Li, Lixiang Li, Jian Zhang

PII: S1056-8727(17)30990-X
DOI: doi: 10.1016/j.jdiacomp.2017.08.011
Reference: JDC 7087

To appear in: *Journal of Diabetes and Its Complications*

Received date: 10 July 2017
Revised date: 19 August 2017
Accepted date: 22 August 2017

Please cite this article as: Gao, Y.-X., Man, Q., Jia, S., Li, Y., Li, L. & Zhang, J., The fasting serum triglyceride levels of elderly population with different progression stages of diabetes mellitus in China, *Journal of Diabetes and Its Complications* (2017), doi: 10.1016/j.jdiacomp.2017.08.011

The fasting serum triglyceride levels of elderly population with different progression stages of diabetes mellitus in China

Yi-Xiong Gao [a], Qingqing Man [a], Shanshan Jia [a], Yuqian Li [a], Lixiang Li [a], Jian Zhang [a,*]

[a] National Institute for Nutrition and Health, Chinese Center for Disease Control and Prevention, No. 29, Nanwei Road, Peking 100050, China

* Corresponding author at: National Institute for Nutrition and Health, Chinese Center for Disease Control and Prevention, No. 29, Nanwei Road, Peking 100050, China. Tel.: +86 010 66237147.

E-mail address: zhjian6708@aliyun.com (J. Zhang).

Abstract

Aims: This cross-sectional study aimed to investigate triglyceride level among Chinese elderly population with different diabetic progressions and related factors of triglyceride.

Methods: Study participants (≥65 years) were recruited from a nationwide cross-sectional surveillance and were divided into four subgroups according to diabetic progression. Their information was obtained via questionnaire and physical examination. Their lipids in fasting serum samples were analyzed.

Results: The serum triglyceride levels (mmol/L, mean±SD) were 1.3±0.8 (subgroup of no prediabetes and no DM), 1.5±1.0 (subgroup of prediabetes), 1.6±1.1 (subgroup of newly diagnosed DM) and 1.7±1.1 (subgroup of previously diagnosed DM), respectively. Only one female participant had a higher triglyceride than upper limit for prevention of acute pancreatitis (11.0 mmol/L). However, 23.1% of participants and 34.8% of DM participants had higher triglyceride than upper limit for prevention of cardiovascular diseases (<1.7 mmol/L). Triglyceride level was positively correlated with diabetic progression (r_s=0.17, p<0.01). Age, gender, waist-to-height ratio (rather than BMI), systolic pressure, serum total cholesterol and HDL-C levels were statistically correlated with triglyceride level for total participants (R^2=0.39, p<0.01).

Conclusions: Aggravation of serum triglyceride level was related to diabetic progression in Chinese elderly population. Triglyceride control was unsatisfactory in Chinese elderly population, especially in elderly population with DM.

Keywords: triglyceride; prediabetes; diabetes mellitus; waist-to-height ratio

1. Introduction

Because of the high prevalence and the severity of health effects in elderly population, diabetes mellitus (DM) is becoming a crucial public health issue in China. It was estimated that approximately 25% of elderly population have DM,[1] and the prevalence of type 2 DM in Chinese elderly population (≥60 years) was 20.4% between 2007 and 2008.[2] Data from "global burden of disease study 2010" showed DM caused 160.1 (95% uncertainty interval: 123.7-176.2) thousand deaths in 2010 in China, which provided over 1.9% of total deaths caused by 231 statistical diseases / injuries.[3] Furthermore, old DM patients had higher rates of coexisting illnesses, such as cardiovascular diseases (CVDs), than other old adults.[1] Prediabetes, which contained impaired fasting glucose (IFG) and impaired glucose tolerance (IGT), was considered as a transitional phase from normal glycemic metabolism to DM and

indicated an increased risk for the future progression of DM.[4] The estimated prevalence of prediabetes in Chinese adults was 50.1%,[5] which indicated the prevalence of DM in China would still increase in decades.

Hypertriglyceridemia was often regarded as an epiphenomenon of metabolic syndrome, which subsequently developed into DM.[6] However, recent study revealed that sustained increment of serum triglyceride (TG) was an independent risk factor for DM and prediabetes, even the level of TG was in the accepted normal range.[7] The elevated TG also interacted with other risk factors in promotion of DM.[8] Furthermore, hypertriglyceridemia can promote CVDs, especially for person with DM,[6,9] and it would be a more important risk factor of CVDs than other dyslipidemia in Asian population.[10] Acute pancreatitis (AP) was another consequence of hypertriglyceridemia,[11] which accounts for 1% to 4% of total cases of AP.[12] Standards of medical care in diabetes (2017) drafted by American Diabetes Association pointed out that the DM patients with severe hypertriglyceridemia (fasting TG level >1000 mg/dL) would receive pharmacological therapy to reduce the risk of AP.[11] In China, type 2 DM patient's upper limits of fasting TG for prevention of AP and of CVDs were 11.0 mmol/L and <1.7 mmol/L, respectively,[2] and general adult's cut point of desirable fasting TG for prevention of CVDs was also <1.7 mmol/L.[13]

Various factors were related to TG level, such as gene polymorphisms,[14,15,16] insulin resistance,[17] alcohol abuse,[18] and abnormal dietary patterns.[19,20] Obviously, the research on related factors of TG would be helpful to determine the main reasons of hypertriglyceridemia in further prospective study, and also would contribute to discover other abnormalities if hypertriglyceridemia was diagnosed.

Because of the aforementioned relationships among TG level, DM and diabetic coexisting illnesses, DM would progress with gradually elevated TG level. However, the nationwide study about TG distribution among elderly population with different diabetic progression in China was not found, and the main reasons of hypertriglyceridemia in Chinese elderly population would be also still unknown. Therefore, relevant data from the first nationwide cross-sectional nutrition and health surveillance of China (2010-2012) were examined in this study to investigate the distribution and to analyze the related factors of serum TG in Chinese elderly population.

2. Study participants, Materials and Methods

2.1. Study participants

A national representative sample of Chinese general population was selected by the nutrition and

health surveillance. In brief, 150 survey sites (i.e. 150 districts / counties), which covered major geographic areas of all 31 provincial level administrative units in mainland China, were determined. All survey sites were stratified by four socioeconomic locations: metropolis (34 survey sites), small and mid-sized cities (41 survey sites), general rural area (45 survey sites) and poor rural area (30 survey sites). Six communities / villages were selected from each survey site based on population proportionate sampling and then 75 families were selected randomly from each community / village. The elderly members (≥65 years) from all selected families who had no previously diagnosed dyslipidemia were defined as the participants of this study (those who had previously diagnosed dyslipidemia were excluded, because the type of previously diagnosed dyslipidemia did not distinguish in the surveillance). The study was conducted according to the guidelines laid down in the Declaration of Helsinki and its successive amendments. All procedures were approved by the Ethical Committee of the Chinese Centre for Disease Control and Prevention. Written informed consents were obtained from all study participants.

All study participants were required to complete an investigator-led questionnaire about their basic and health information. Moreover, all selected families belonged to the same community / village were divided into three groups (25 families / group) according to the geographic distance among them, and the study participants from one random group out of the three groups were required to complete an additional food frequency questionnaire (FFQ), which included the information on their consumption of common food in the latest year and of culinary oil in the latest month. The common food listed in the FFQ was classified as the following categories in this study: staple foods, marine fish, freshwater fish, shellfish, meat / poultry, animal organs, eggs, milk / dairy products, vegetables and fruits.

2.2. Physical examination

All study participants completed a physical examination after an overnight fast of 10 ~ 14 hours. The examination included measurements of height, fasting body weight, fasting waist circumference and blood pressure. Body mass index (BMI) was calculated according to height and fasting body weight. Fasting waist circumference of each study participant was measured 2 times and the mean was calculated as the participant's fasting waist circumference. Waist-to-height ratio (WHtR) was defined as fasting waist circumference (cm) divided by height (cm), and abdominal obesity was defined as a WHtR of 0.60 or higher in this study, because fasting waist circumference "does not take differences in height into account".[21] Systolic and diastolic pressures were measured consecutively at right arm 3

times with a 30-seconds interval between measurements with the participant in a seated position after 5 minutes of rest by adjusted mercury sphygmomanometer, and then the mean of blood pressure was calculated.

2.3. Clinical and biochemical measurement

The fasting blood samples were collected during the physical examination, and the serum was processed via centrifugation (1500 g, 15 min). Study participants without previously diagnosed DM accepted an additional oral glucose tolerance test. Their blood samples were re-collected at 2 hours after the intake of 75 g glucose dissolved in 300 ml water, and their serum was processed by aforementioned method. The concentrations of TG, glucose, total cholesterol (TC) and high density lipoprotein cholesterol (HDL-C) in serum were analyzed by GPO-HMMPS glycerol blanking method, hexokinase G-6-PDH method, cholesterol oxidase-HMMPS method and direct determination method, respectively. All analyses were executed by Hitachi 7600 automated biochemical analyzer, and all reagents were produced by Wako Pure Chemical, Ltd. According to China guideline for type 2 diabetes, DM was defined as a fasting plasma glucose (FPG) of 7.0 mmol/L or higher, or oral glucose tolerance test 2 hours-plasma glucose (OGTT 2h-PG) of 11.1 mmol/L or higher; IFG was defined as a FPG of 6.1 mmol/L to 7.0 mmol/L and an OGTT 2h-PG of which the value was lower than 7.8 mmol/L; IGT was defined as a FPG of which the value was lower than 7.0 mmol/L and an OGTT 2h-PG of 7.8 mmol/L to 11.1 mmol/L; a participant who suffered from IFG or IGT was defined as a prediabetic participant.[2] In this study, the concentration of glucose in serum was applied to be as the diagnostic criteria of DM, IFG and IGT, because the plasma samples for glycemic analysis were unavailable. The upper limit of fasting serum TG for prevention of CVDs was <1.7 mmol/L,[2,13] and of AP was 11.0 mmol/L.[2] Study participants whose TG level exceeded these upper limits were considered to be at high risk of CVDs or AP in this study.

Study participants were divided into four subgroups according to their progression stages of DM: subgroup of no prediabetes and no DM, subgroup of prediabetes, subgroup of newly diagnosed DM, and subgroup of previously diagnosed DM.

2.4. Statistical analysis

Continuous variables were expressed as means and standard deviation (SD) according to central limit theorem, because the number of study participants of each subgroup was sufficiently large. Categorical variables were expressed as percentages. Chi-square test was applied to analyze the

differences of prevalence among subgroups. Cochran-Armitage test for trend was applied to analyze if prevalence increased / decreased with diabetic progression. The application of t test or satterthwaite t test for analysis of the differences between two genders was depended on whether variances are equal or not. ANOVA or Kruskal-Wallis test was applied to analyze the differences of continuous variables among subgroups, and Student-Newman-Keuls test or Dwass-Steel-Critchlow-Fligner method was applied to analyze intergroup differences according to whether variances are equal or not. Spearman's rank correlation (r_s) was applied to access the relationship between continuous and rank variables. The statistically significant related factors of serum TG were analyzed by multiple linear regression with stepwise selection method. A value for $p<0.05$ was considered to indicate statistical significance. All statistical analyses were carried out by Statistical Analysis System 9.3 (SAS Institute Inc., Cary, NC, U.S.).

3. Results

3.1. Information on study participants

This study recruited 15744 participants, which provided 78.3% of elderly surveillance participants (the other 21.7% of elderly surveillance participants had previously diagnosed dyslipidemia (n=1425), or did not complete questionnaire and / or physical examination). The study participants numbers of four subgroups were 10495 (subgroup of no prediabetes and no DM), 2783 (subgroup of prediabetes), 1099 (subgroup of newly diagnosed DM), and 1367 (subgroup of previously diagnosed DM), respectively. The prediabetes and DM patients provided 17.7% and 15.7% of total study participants, respectively. The female prevalence of prediabetes ($p<0.01$) and DM ($p<0.01$) were statistically higher than male prevalence. The prevalence of previously diagnosed DM of metropolis was statistically higher than of other locations ($p<0.01$), and the prevalence gradually increased in order of poor rural area, general rural area, small / mid-sized cities and metropolis (p for trend: <0.01). There was no statistical difference among four locations with respect to the prevalence of newly diagnosed DM ($p=0.54$). The study participants from general rural area had the highest prevalence of prediabetes ($p<0.01$). Relevant information was presented in Table 1.

3.2. Results of physical examination

The concentrations of fasting serum glucose of study participants with newly and previously diagnosed DM were 7.6±2.1 mmol/L and 7.6±2.6 mmol/L, respectively, and there was no statistical difference between them ($p=0.66$). Over 80% of study participants with previously diagnosed DM

accepted pharmacologic treatment (n=1146). However, over half of participants with previously diagnosed DM had an over-limit fasting serum glucose (n=690), and 52.5% of participants with previously diagnosed DM who accepted pharmacologic treatment still had an over-limit fasting serum glucose (n=602).

There was no statistical difference of prevalence of underweight (BMI≤18.5) between two genders (men: 7.36%; women: 6.96%; p=0.34). However, female BMI (23.8±3.8) and WHtR (0.54±0.07) were statistically higher than male BMI (23.1±3.3) and WHtR (0.51±0.06) (p<0.01, for both BMI and WHtR). The prevalence of abdominal obesity was 9.3% (subgroup of no prediabetes and no DM), 14.8% (subgroup of prediabetes), 17.8% (subgroup of newly diagnosed DM), and 20.8% (subgroup of previously diagnosed DM), respectively, and the prevalence increased with the progression of DM (p for trend: <0.01). The subgroup of previously diagnosed DM had the highest height (p<0.01), fasting body weight (p<0.01), fasting waist circumference (p<0.01), BMI (p<0.01), WHtR (p<0.01), and the lowest fasting serum HDL-C (p<0.01). The WHtR was positively correlated with diabetic progression (total study participants: r_s=0.21, p<0.01; men: r_s=0.22, p<0.01; women: r_s=0.18, p<0.01). The results of physical examination were presented in Table 2.

3.3. Dietary information

A total of 4653 study participants completed the FFQ (men: 2337; women: 2316). The numbers of study participants without prediabetes and DM, with prediabetes, with newly diagnosed DM, and with previously diagnosed DM were 3064, 843, 344, 402, respectively. The main culinary oil consumed by investigated study participants were rapeseed oil, soybean oil, arachis oil and animal fats. These oils provided 95.0% of total consumption of culinary oil. There were no statistical differences among subgroups with respect to consumption of freshwater fish (p=0.48), animal organs (p=0.44), vegetables (p=0.09), soybean oil (p=0.06) and arachis oil (p=0.05). The dietary pattern of subgroup of previously diagnosed DM was significantly different with of other subgroups: this subgroup had the lowest average consumption of staple foods (1853 g/week, p<0.01), fruits (578 g/week, p=0.03), rapeseed oil (53 g/week, p=0.03) and animal fats (10 g/week, p<0.01), but the highest average consumption of marine fish (97 g/week, p<0.01), shellfish (46 g/week, p<0.01), meat / poultry (483 g/week, p<0.01), eggs (288 g/week, p<0.01) and milk / dairy products (613 g/week, p<0.01).

3.4. Fasting serum TG level

There was only one study participant whose serum TG was higher than upper limit for prevention of

AP (11.0 mmol/L). Her serum TG was 11.3 mmol/L and she was from the subgroup of previously diagnosed DM.

The prevalence of study participants with higher serum TG than upper limit for prevention of CVDs (<1.7 mmol/L) were 19.0% (subgroup of no prediabetes and no DM), 28.3% (subgroup of prediabetes), 33.0% (subgroup of newly diagnosed DM), and 36.2% (subgroup of previously diagnosed DM), respectively. This prevalence increased with the progression of DM (Figure 1, p for trend: <0.01, for total study participants, male and female participants, respectively). The prevalence was 23.1% in total study participants and 34.8% in study participants with DM (including previously and newly diagnosed DM).

The TG level of two DM subgroups was statistically higher than of other subgroups ($p<0.01$), and there was no statistical difference between two DM subgroups ($p=0.13$). Female means of serum TG were statistically higher than male means in each subgroup ($p<0.01$ for each subgroup). The serum TG level was positively correlated with the progression of DM (total study participants: $r_s=0.17$, $p<0.01$; male study participants: $r_s=0.15$, $p<0.01$; female study participants: $r_s=0.17$, $p<0.01$). More detailed information on serum TG level among different subgroups was presented in Table 3.

3.5. Related factors of fasting serum TG

Age, gender, BMI, WHtR, systolic pressure, diastolic pressure, fasting serum TC, fasting serum HDL-C and all food categories / culinary oil listed in subsection 3.3 were regarded as potential related factors of fasting serum TG in this study.

Information on age, gender, BMI, WHtR, systolic pressure, diastolic pressure, fasting serum TC and fasting serum HDL-C were available from total study participants (n=15744). The model was adjusted by fasting serum glucose. Age, gender, WHtR, systolic pressure, fasting serum TC and fasting serum HDL-C were statistically significant related factors of fasting serum TG (p for the model: <0.01, $R^2=0.39$). BMI and diastolic pressure did not enter into the model.

Information on age, gender, BMI, WHtR, systolic pressure, diastolic pressure, fasting serum TC and fasting serum HDL-C were available from study participants who accepted OGTT-2hPG (n=14377, study participants with previously diagnosed DM did not experience OGTT). The model was adjusted by fasting serum glucose and OGTT-2hPG. The statistically significant related factors of this model were exactly the same as the factors of the model for total study participants (p for the model: <0.01, $R^2=0.39$). BMI and diastolic pressure did not enter into the model.

Information on age, gender, BMI, WHtR, systolic pressure, diastolic pressure, fasting serum TC, fasting serum HDL-C and all food categories / culinary oil listed in subsection 3.3 were available from study participants who accepted FFQ (n=4653). The model was adjusted by fasting serum glucose. The statistically significant related factors of this model were exactly the same as the factors of the model for total study participants (p for the model: <0.01, R^2=0.39). BMI, diastolic pressure and all food categories / culinary oil listed in subsection 3.3 did not enter into the model.

The information on models for total study participants (n=15744) and for study participants who accepted OGTT (n=14377) was presented in Table 4.

4. Discussion

Hypertriglyceridemia is the risk factor of both DM and CVDs.[6,7,9] Meanwhile, DM was also a definite risk factor of CVDs,[22] and the increment of fasting and postprandial plasma glucose were also associated with an increased risk for CVDs, even though the person did not suffer from DM.[23] All of these demonstrated the direct and indirect pathogenesis of TG in promotion of CVDs. Furthermore, the hypertriglyceridemia-induced lipid deposit in pancreas was supposed to play a crucial role in progression of AP.[24] The increment of lipase activity during AP resulted in accelerated decomposition of fat tissue with subsequent release of TG in blood,[25] which formed the vicious circle and further aggravated AP. Our results showed that only one woman from total of 15744 study participants had higher serum TG concentration than upper limit for prevention of AP, which indicated that Chinese elderly population without previously diagnosed dyslipidemia would have relatively low risk of AP. However, over 30% of DM participants and over 20% of total study participants had high risk to suffer from TG-related CVDs, and the TG level of participants with previously diagnosed DM was as high as the level of participants with newly diagnosed DM, all of these indicated that the control of TG appeared to be unsatisfactory in Chinese elderly population, especially in elderly population with DM.

The questionnaire just investigated if the surveillance participants suffered from dyslipidemia, but did not distinguish the type of previously diagnosed dyslipidemia, which meant that the information from surveillance participants with previously diagnosed dyslipidemia would be confounding factor during the analysis of related factors of serum TG, because we can not determine if their serum TG was affected by some unknown factors, such as TG-lowering agents. Therefore, these surveillance participants were excluded from this study.

There is no United Nations (UN) standard numerical criterion of an elderly or older person, and the

UN agreed cutoff is 60+ years to refer to the older population.[26] Taking into account the fact that "most developed world countries have accepted the chronological age of 65 years as a definition of 'elderly' or older person",[26] we applied 65 years as the cutoff to define elderly person in this study, because we considered that our results would be comparable with other similar studies around the world.

The relatively high rate of pharmacologic treatment and the significantly different dietary pattern compared to other subgroups indicated that study participants with previously diagnosed DM were concerned about their health conditions and took measures to respond to DM. However, over half of those participants still had an over-limit fasting blood glucose, and there was no statistical difference of fasting serum glucose between subgroups of newly and previously diagnosed DM, which indicated that the glycemic control in Chinese elderly DM patients appeared to be unsatisfactory.

All study participants would not take active measures to control their TG because they had no previously diagnosed dyslipidemia, however, glucose-lowering medications had various effects on TG level: some of them exerted TG-lowering effects (e.g. exenatide[27] and pioglitazone[28]), and some other elevated TG level (e.g. bile acid sequestrants[6,28]). The surveillance questionnaires did not refer to the type of glucose-lowering medications. Therefore, the effects of these medications on TG can not be assessed in this study. However, the unsatisfactory glycemic control in subgroup of previously diagnosed DM indicated the effect of pharmacologic treatment appeared to be slight in this study.

Marine-derived n-3 polyunsaturated fatty acids (n-3 PUFAs), but not plant-based n-3 PUFAs, actually exert TG-lowering effects in many cases.[6,29] There were various mechanisms of action of marine-derived n-3 PUFAs, for example, EPA and DHA can suppress SREBP-1,[30] and regulate the expression levels of some enzymes which play crucial roles in endogenous synthesis of TG.[15] These indicated that participants who had higher consumption of marine fish would be more likely to have a relatively low serum TG level. However, n-3 PUFA supplementation appeared to be not always effective,[31] because some other factors may attenuate or eliminate marine-derived n-3 PUFA-induced effects, such as single nucleotide polymorphisms.[14,15,16] Furthermore, some fat-soluble contaminants existed in edible part of marine fish (e.g. DLCs) may impair lipid metabolism,[32] which would counteract the benefits from n-3 PUFAs. The concentrations of some fat-soluble contaminants tended to be relatively high in some marine fish.[33,34] These could partially be the reasons why marine fish consumption could not affect serum TG in our study. All of the aforementioned facts indicated that benefit risk assessment and species-specific effects would be considered during the dietary

recommendation of marine fish.

The endogenous metabolisms of lipids and glucose, and systolic pressure can be affected by same factors.[27,35] "Glycemic control may also beneficially modify plasma lipid levels", particularly in DM patients with high TG.[10] These would be the reason why systolic pressure, some blood lipids (e.g. fasting serum HDL-C) and diabetic progression were correlated with fasting serum TG in this study. The correlation indicated that TG level would result from the interactions of many metabolic components in vivo, and TG level would be as an indicator of holistic health condition. Therefore, although metabolic disorder of TG is the most obvious characteristic of persons with hypertriglyceridemia, these persons would also concern metabolic abnormalities of other components.

An effective obesity management can delay the progression of DM and also produce clinically meaningful reduction in TG in type 2 DM patients.[36] Our study showed that WHtR, rather than BMI, was statistically significant related factor of serum TG, which indicated a higher TG level would be related to abdominal obesity rather than general obesity in Chinese elderly population. For the reason for carefulness, study participants should concern their body weight and waist circumference to avoid any type of obesity, especially those participants with DM. There was statistical correlation between WHtR and BMI ($r=0.78$, $p<0.01$), which would be the reason why BMI would be a statistically significant related factor of serum TG if WHtR was unavailable (beta=0.01, $p<0.01$).

Estrogen could regulate lipid metabolism via partition of lipid metabolism toward oxidation and away from storage in the form of TG.[37] Female elderly people appeared to be more prone to suffer from menopause-mediated endocrine disorders, for example, the prevalence of obesity in female elderly people was statistically higher than in male counterparts.[38] Our results also found higher BMI and WHtR in female participants, which was in general accordance with the aforementioned study. Therefore, the change of secretion of estrogen would be the reason why female was a risk factor for elevated serum TG in elderly population.

An interesting discovery of this study was that serum TG level was negatively correlated with age in elderly population. However, we do not regard older age as a protective factor. Actually, we considered that the senility may attenuate the capability of lipid metabolism, including the capability of endogenous synthesis of TG, though the detailed mechanism remains to be studied. Our data showed that both fasting serum TC ($p=0.27$) and HDL-C ($p=0.08$) had no correlation with age among elderly people (These did not presented as results in this article), which indicated that senility would affect

metabolism of TG to a larger extent than of other blood lipids.

In conclusion, the current study found that the diabetic progression was positively related to the elevated TG level in Chinese elderly population. Chinese elderly population without previously diagnosed dyslipidemia would have relatively low risk of severe-hypertriglyceridemia-induced AP. However, over 20% of them had relatively high risk to suffer from TG-related CVDs, and the prevalence was even higher (over 30%) in subpopulation of DM. These showed that TG control was unsatisfactory in Chinese elderly population, especially in elderly population with DM. Age, genders, abdominal obesity (rather than general obesity), systolic pressure, fasting serum TC and HDL-C were statistically related to fasting serum TG in elderly population in China.

Acknowledgments

This study was financially supported by National Natural Science Foundation of China (No. 81602857). Dr. Hailing Chen from Beijing Jishuitan Hospital provided clinical information on prediabetes and DM. We thank all participants and investigators from the surveillance.

References

1. American Diabetes Association. Standards of medical care in diabetes 2017: Section 11. Older adults. Diabetes Care. 2017; 40: S99-S104.
2. Chinese Diabetes Society. China guideline for type 2 diabetes. Peking, Peking University Medical Press: 2013. ISBN: 978-7-5659-0942-9. (Published in Chinese)
3. Yang G, Wang Y, Zeng Y, Gao GF, Liang X, Zhou M, et al. Rapid health transition in China, 1990-2010: findings from the global burden of disease study 2010. Lancet. 2013; 381: 1987-2015.
4. American Diabetes Association. Standards of medical care in diabetes 2017: Section 2. Classification and diagnosis of diabetes. Diabetes Care. 2017; 40: S11-S24.
5. Xu Y, Wang L, He J, Bi Y, Li M, Wang T, et al. Prevalence and control of diabetes in Chinese adults. JAMA. 2013; 310: 948-959.
6. Miller M, Stone NJ, Ballantyne C, Bittner V, Criqui MH, Ginsberg HN, et al. Triglycerides and cardiovascular disease: a scientific statement from the American Heart Association. Circulation. 2011; 123: 2292-2333.
7. Beshara A, Cohen E, Goldberg E, Lilos P, Garty M, Krause I. Triglyceride levels and risk of type 2 diabetes mellitus: a longitudinal large study. J Investig Med. 2016; 64: 383-387.
8. Zou D, Ye Y, Zou N, Yu J. Analysis of risk factors and their interactions in type 2 diabetes mellitus: a

cross-sectional survey in Guilin, China. J Diabetes Investig. 2017; 8: 188-194.

9. Ko GT, Chan JC, Chow CC, Yeung VT, Chan WB, So WY, et al. Triglyceride, albuminuria and blood pressure are the major associations of non-fatal cardiovascular disease in Chinese type 2 diabetes. Acta Diabetol. 2003; 40: 80-84.
10. Chen AH, Tseng CH. The role of triglyceride in cardiovascular disease in asian patients with type 2 diabetes - a systematic review. The Review of Diabetic Studies. 2013; 10: 101-109.
11. American Diabetes Association. Standards of medical care in diabetes 2017: Section 9. Cardiovascular disease and risk management. Diabetes Care. 2017; 40: S75-S87.
12. Tariq H, Gaduputi V, Peralta R, Abbas N, Nayudu SK, Thet P, et al. Serum Triglyceride Level: A Predictor of Complications and Outcomes in Acute Pancreatitis? Can J Gastroenterol Hepatol. 2016; 2016: 8198047.
13. Zhong guo cheng ren xue zhi yi chang fang zhi zhi nan xiu ding lian he wei yuan hui. Zhong guo cheng ren xue zhi yi chang fang zhi zhi nan (2016). Chinese Circulation Journal. 2016; 31: 937-953. (Published in Chinese)
14. Yang J, Gao Q, Gao X, Tao X, Cai H, Fan Y, et al. Melanocortin-4 receptor rs17782313 polymorphisms are associated with serum triglycerides in older Chinese women. Asia Pac J Clin Nutr. 2016; 25: 213-219.
15. Ouellette C, Cormier H, Rudkowska I, Guénard F, Lemieux S, Couture P, et al. Polymorphisms in genes involved in the triglyceride synthesis pathway and marine omega-3 polyunsaturated fatty acid supplementation modulate plasma triglyceride levels. J Nutrigenet Nutrigenomics. 2013; 6: 268-280.
16. Rudkowska I, Guénard F, Julien P, Couture P, Lemieux S, Barbier O, et al. Genome-wide association study of the plasma triglyceride response to an n-3 polyunsaturated fatty acid supplementation. J Lipid Res. 2014; 55: 1245-1253.
17. Lin D, Qi Y, Huang C, Wu M, Wang C, Li F, et al. Associations of lipid parameters with insulin resistance and diabetes: A population-based study. Clin Nutr. 2017; doi: 10.1016/j.clnu.2017.06.018.
18. Bessembinders K, Wielders J, van de Wiel A. Severe hypertriglyceridemia influenced by alcohol (SHIBA). Alcohol Alcohol. 2011; 46: 113-116.
19. Silva ME, Pupo AA, Ursich MJ. Effects of a high-carbohydrate diet on blood glucose, insulin and

triglyceride levels in normal and obese subjects and in obese subjects with impaired glucose tolerance. Braz J Med Biol Res. 1987; 20: 339-350.

20. Pejic RN, Lee DT. Hypertriglyceridemia. J Am Board Fam Med. 2006; 19: 310-316.

21. Schneider HJ, Klotsche J, Silber S, Stalla GK, Wittchen HU. Measuring abdominal obesity: effects of height on distribution of cardiometabolic risk factors risk using waist circumference and waist-to-height ratio. Diabetes Care. 2011; 34: e7.

22. Barr EL, Cunningham J, Tatipata S, Dunbar T, Kangaharan N, Guthridge S, et al. Associations of mortality and cardiovascular disease risks with diabetes and albuminuria in urban Indigenous Australians: the DRUID follow-up study. Diabet Med. 2017; doi: 10.1111/dme.13360.

23. Sanusi H. Impaired glucose tolerance, impaired fasting glycaemia and cardiovascular risk. Acta Med Indones. 2004; 36: 36-41.

24. Toskes PP. Hyperlipidemic pancreatitis. Gastroenterol Clin North Am. 1990; 19: 783-791.

25. Cheng L, Luo Z, Xiang K, Ren J, Huang Z, Tang L, et al. Clinical significance of serum triglyceride elevation at early stage of acute biliary pancreatitis. BMC Gastroenterol. 2015; 15: 19.

26. World Health Organization. Proposed working definition of an older person in Africa for the MDS Project. http://www.who.int/healthinfo/survey/ageingdefnolder/en/.

27. Varanasi A, Chaudhuri A, Dhindsa S, Arora A, Lohano T, Vora MR, et al. Durability of effects of exenatide treatment on glycemic control, body weight, systolic blood pressure, C-reactive protein, and triglyceride concentrations. Endocr Pract. 2011; 17: 192-200.

28. American Diabetes Association. Standards of medical care in diabetes 2017: Section 8. Pharmacologic approaches to glycemic treatment. Diabetes Care. 2017; 40: S64-S74.

29. Weber P, Raederstorff D. Triglyceride-lowering effect of omega-3 LC-polyunsaturated fatty acids - a review. Nutr Metab Cardiovasc Dis. 2000; 10: 28-37.

30. Chin HJ, Fu YY, Ahn JM, Na KY, Kim YS, Kim S, et al. Omacor, n-3 polyunsaturated fatty acid, attenuated albuminuria and renal dysfunction with decrease of SREBP-1 expression and triglyceride amount in the kidney of type II diabetic animals. Nephrol Dial Transplant. 2010; 25: 1450-1457.

31. Tremblay AJ, Lamarche B, Hogue JC, Couture P. N-3 polyunsaturated fatty acid supplementation has no effect on postprandial triglyceride-rich lipoprotein kinetics in men with type 2 diabetes. J Diabetes Res. 2016; 2016: 2909210.

32. Duval C, Teixeira-Clerc F, Leblanc AF, Touch S, Emond C, Guerre-Millo M, et al. Chronic Exposure to Low Doses of Dioxin Promotes Liver Fibrosis Development in the C57BL6/J Diet-Induced Obesity Mouse Model. Environ Health Perspect. 2016; DOI: 10.1289/EHP316.

33. Gao YX, Zhang H, Yu X, He JL, Shang X, Li X, et al. Risk and benefit assessment of potential neurodevelopmental effect resulting from consumption of marine fish from a coastal archipelago in China. J Agric Food Chem. 2014; 62: 5207-5213.

34. Gao YX, Zhang HX, Li JG, Zhang L, Yu XW, He JL, et al. The Benefit Risk Assessment of Consumption of Marine Species Based on Benefit-Risk Analysis for Foods (BRAFO)-tiered Approach. Biomed Environ Sci. 2015; 28: 243-252.

35. Raimondo A, Rees MG, Gloyn AL. Glucokinase regulatory protein: complexity at the crossroads of triglyceride and glucose metabolism. Curr Opin Lipidol. 2015; 26: 88-95.

36. American Diabetes Association. Standards of medical care in diabetes 2017: Section 7. Obesity management for the treatment of type 2 diabetes. Diabetes Care. 2017; 40: S57-S63.

37. D'Eon TM, Souza SC, Aronovitz M, Obin MS, Fried SK, Greenberg AS. Estrogen regulation of adiposity and fuel partitioning. Evidence of genomic and non-genomic regulation of lipogenic and oxidative pathways. J Biol Chem. 2005; 280: 35983-35991.

38. Li ZB, Ho SY, Chan WM, Ho KS, Li MP, Leung GM, et al. Obesity and depressive symptoms in Chinese elderly. Int J Geriatr Psychiatry. 2004; 19: 68-74.

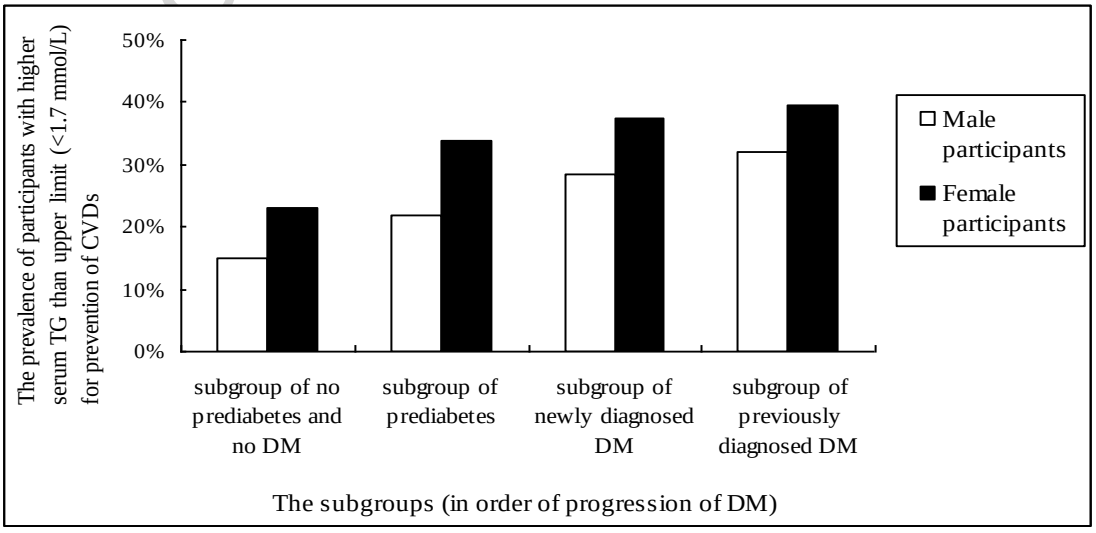

Figure 1. The correlation between prevalence of participants with higher serum TG than upper limit for prevention of CVDs (%) and progression of DM

Table 1. Demographics of study participants (n=15744)

	Number of study participants	Subgroups (% of the row)			
		no prediabetes and no DM	prediabetes	newly diagnosed DM	previously diagnosed DM
Gender					
Men	7759	68.6	16.8	6.9	7.8
Women	7985	64.8	18.6	7.1	9.6
Ethnic groups					
Han	14667	65.8	18.0	7.2	8.9
The other ethnic groups	1077	77.8	12.7	3.9	5.6
Age intervals (years)					
65~	6733	69.5	16.3	6.5	7.7
70~	4798	65.4	18.0	6.6	9.9
75~	2859	65.4	18.6	7.1	8.8
80~	1354	59.7	21.3	10.1	8.9
Locations					
Metropolis	3639	58.1	17.4	7.1	17.4
Small/mid-sized cities	4721	66.5	17.1	7.3	9.0
General rural area	4989	68.5	19.6	6.8	5.1
Poor rural area	2395	76.2	15.1	6.5	2.2

Table 2. Information on physical examination of study participants from different subgroups (n=15744)

	Gender	Subgroups							
		no prediabetes and no DM		prediabetes		newly diagnosed DM		previously diagnosed DM	
		mean	SD	mean	SD	mean	SD	mean	SD
Height (cm)	Overall	157.4 b	8.7	156.5 c	8.6	156.8 c	8.7	158.7 a	8.4
	Men	163.1 b	6.7	162.6 b	6.9	162.8 b	6.5	165.2 a	6.4
	Women	151.5 b	6.4	151.2 b	6.0	151.1 b	6.3	153.6 a	5.9
Fasting body	Overall	57.4 d	10.8	58.6 c	11.2	60.3 b	12.0	63.4 a	10.5
weight (kg)	Men	60.7 d	10.4	62.4 c	11.1	63.9 b	11.8	68.0 a	10.0
	Women	53.9 d	10.1	55.4 c	10.3	56.9 b	11.2	59.7 a	9.4
Fasting waist	Overall	80.7 d	10.2	83.3 c	10.4	85.1 b	10.5	87.7 a	9.6
circumference	Men	81.2 d	10.0	83.8 c	10.4	85.7 b	10.4	89.2 a	9.5
(cm)	Women	80.3 d	10.3	82.8 c	10.4	84.5 b	10.5	86.6 a	9.5
BMI	Overall	23.1 d	3.5	23.9 c	3.7	24.4 b	4.0	25.1 a	3.4
	Men	22.8 d	3.2	23.5 c	3.5	24.0 b	3.6	24.9 a	3.1
	Women	23.4 d	3.7	24.1 c	3.8	24.8 b	4.2	25.3 a	3.5
WHtR	Overall	0.51 d	0.06	0.53 c	0.07	0.54 b	0.07	0.55 a	0.06
	Men	0.50 d	0.06	0.52 c	0.06	0.53 b	0.06	0.54 a	0.06
	Women	0.53 c	0.07	0.55 b	0.07	0.56 a	0.07	0.56 a	0.06
Systolic	Overall	136 c	22	139 b	22	141 a	22	138 b	22
pressure	Men	135 c	22	138 b	21	140 a	21	136 bc	23
(mmHg)	Women	137 c	22	139 b	22	142 a	24	140 b	22
Diastolic	Overall	79 b	12	80 b	12	81 a	12	78 c	12
pressure	Men	80 b	12	80 ab	12	81 a	12	78 c	12
(mmHg)	Women	79 b	12	80 ab	12	81 a	12	78 c	12
Fasting serum	Overall	4.8 d	1.0	4.9 b	1.0	5.1 a	1.1	4.9 c	1.0
TC (mmol/L)	Men	4.5 c	0.9	4.8 b	0.9	4.9 a	1.1	4.6 c	0.9
	Women	5.0 c	1.0	5.1 ab	1.0	5.2 a	1.1	5.0 bc	1.0
Fasting serum	Overall	1.2 a	0.3	1.2 a	0.4	1.2 b	0.4	1.1 c	0.3
HDL-C	Men	1.2 ab	0.3	1.2 a	0.4	1.2 b	0.4	1.1 c	0.3

(mmol/L)	Women	1.3 a	0.3	1.2 b	0.3	1.2 b	0.3	1.1 c	0.3

The means with different letters in the same row denote statistical differences among subgroups, and the mean values decrease gradually in alphabetical order.

Table 3. Serum TG level (mmol/L) among different subgroups (n=15744)

	Subgroups							
	no prediabetes and no DM		prediabetes		newly diagnosed DM		previously diagnosed DM	
	mean	SD	mean	SD	mean	SD	mean	SD
Overall	1.3 c	0.8	1.5 b	1.0	1.6 a	1.1	1.7 a	1.1
Gender								
Men	1.2 c	0.7	1.3 b	0.9	1.5 a	1.1	1.6 a	1.1
Women	1.4 c	0.8	1.6 b	1.0	1.8 a	1.1	1.8 a	1.1
Age intervals (years)								
65~	1.3 c	0.8	1.6 b	1.1	1.8 a	1.3	1.8 a	1.3
70~	1.3 c	0.8	1.4 b	0.9	1.5 a	1.0	1.6 a	1.0
75~	1.2 c	0.8	1.4 b	1.0	1.6 a	1.2	1.6 a	0.9
80~	1.2 c	0.6	1.3 c	0.7	1.5 b	0.9	1.6 a	1.0
Locations								
Metropolis	1.4 c	0.8	1.6 b	0.8	1.8 a	1.2	1.7 ab	1.1
Small / mid-sized cities	1.3 c	0.8	1.4 b	0.9	1.7 a	1.1	1.7 a	1.0
General rural area	1.2 d	0.8	1.4 c	1.0	1.6 b	1.3	1.8 a	1.1
Pool rural area	1.2 b	0.8	1.4 b	1.1	1.3 b	0.9	1.9 a	1.6

The means with different letters in the same row denote statistical differences among subgroups, and the mean values decrease gradually in alphabetical order.

Table 4. The statistically significant related factors of serum TG

Related factors and intercept	Model for total study participants (n=15744, adjusted by fasting serum glucose)			Model for study participants except for subgroup of previously diagnosed DM (n=14377, adjusted by fasting serum glucose and OGTT-2hPG)		
	Beta	P valve	Standardized beta	Beta	P valve	Standardized beta
Age (years)	-0.01	<0.01	-0.05	-0.01	<0.01	-0.05
Female participants[a]	0.11	<0.01	0.06	0.11	<0.01	0.06
WHtR	0.61	<0.01	0.05	0.56	<0.01	0.04
Fasting serum TC (mmol/L)	0.38	<0.01	0.42	0.37	<0.01	0.42
Fasting serum HDL-C (mmol/L)	-1.39	<0.01	-0.53	-1.33	<0.01	-0.53
Systolic pressure (mmHg)	0.001	<0.01	0.03	0.001	<0.01	0.04
Intercept[b]	0.86	<0.01	-	0.94	<0.01	-

[a] The reference group was male participants.

[b] The "-" in the row of intercept denotes that intercept has no standardized beta.

Highlights

1. This study found aggravation of fasting serum triglyceride level was related to diabetic progression in a national representative elderly population (≥65 years) of China.
2. The TG control was unsatisfactory in Chinese elderly population, especially in elderly population with DM.
3. The statistically significant related factors of fasting serum TG were age, gender, waist-to-height ratio (rather than BMI), systolic pressure, fasting serum total cholesterol and fasting serum high density lipoprotein cholesterol in the national representative elderly population.