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Title

A retrospective database study to explore multimorbidity among patients with type 2 diabetes in a tertiary care department in Ningbo, China

Xueyu Li*[1, 2], Kaushik Chattopadhyay*[3], Shengnan Xu[1], Yanshu Chen[1], Miao Xu[1], Li Li[1], Jialin Li[1]

[1]Department of Endocrinology and Metabolism, Ningbo First Hospital, Ningbo, PR China

[2]Ningbo University Medical School, Ningbo, PR China

[3]Division of Epidemiology and Public Health, School of Medicine, University of Nottingham, Nottingham, UK

*These authors contributed equally to this work.

Corresponding author: Dr Jialin Li, e-mail; lijialin@sina.com

Abstract

Objectives To determine the prevalence of multimorbidity among type 2 diabetes (T2DM) patients and factors independently associated with multimorbidity in a tertiary care department in Ningbo, China.

Design A computerised medical records database was used to conduct a retrospective cross-sectional study.

Setting Tertiary care department in Ningbo, China.

Participants The study included adult patients with T2DM and eight years of data, from 1 January 2012 to 31 December 2019.

Primary outcome measure Multimorbidity which was defined as having T2DM and at least one other chronic condition, each one was either a physical non-communicable disease of long duration (≥3 months), a mental health condition of long duration (≥3 months) or an infectious disease of long duration (≥3 months).

Results 4777 patients satisfied the eligibility criteria. Over eight years, the prevalence of multimorbidity among patients with T2DM was 93.7%. Those who had multimorbidity, the mean (±standard deviation) number of other chronic conditions was 3 (±1). The odds of multimorbidity increased with the age of patients (18-39 years: 1; 40-59 years: odds ratio 2.80, 95% confidence interval 1.97-3.96; and ≥60 years: 6.04, 4.21-8.67). The odds were lower in female patients (0.63, 0.49-0.81), patients residing in rural areas (0.74, 0.58-0.94) and patients without health insurance (0.59, 0.43-0.80). The odds were higher in single/divorced/widowed patients compared to married patients (2.11, 1.32-3.37).

Conclusions A large percentage of patients with T2DM in the tertiary care department in Ningbo, China had multimorbidity and the associated factors were identified. The

findings could be used in developing, evaluating and implementing interventions aimed at improving outcomes in T2DM patients with multimorbidity.

Keywords

Multimorbidity, Type 2 diabetes, China

Strengths and limitations of the study

- Ours was the first study to investigate multimorbidity among patients with type 2 diabetes in Ningbo and in the broader Zhejiang Province and China.
- In our database, all the conditions are coded using the International Classification of Diseases, 10th edition (ICD-10), and we included all the chronic conditions in our study.
- Our study had extremely low missing data and the multiple logistic regression analysis included a sample with missing data for the adjusted variable.
- Being a cross-sectional study, the causal relationship between variables and multimorbidity could not be determined.
- Our study had the usual routinely collected data issues as an existing medical records database was used – its main purpose is medical management and not research.

Introduction

Ningbo is an economically developed Chinese city in the Zhejiang Province. Non-communicable diseases, mental health conditions and infectious diseases are prevalent in the city.[1] One such non-communicable disease is type 2 diabetes (T2DM), a complex metabolic disorder. China has the largest T2DM epidemic in the world, and in Ningbo, its prevalence in 40+ years adults is 21%.[2] In real-life, T2DM is rarely presented in isolation and is accompanied by other chronic conditions.[3]

Globally, research on multimorbidity is a conceptually new area. Multimorbidity is commonly defined as having two or more chronic conditions in the same individual.[4] It accelerates the progression of individual chronic conditions;[5] brings in other physical and mental conditions and even premature mortality;[6 7] negatively affects the overall health, wellbeing and functioning;[8 9] and leads to high treatment burden, healthcare utilisation and expenditure and loss of economic output.[10-13]

To date, no study has been undertaken to investigate multimorbidity among patients with T2DM in Ningbo. The study objectives were to determine the prevalence of multimorbidity among patients with T2DM and factors independently associated with multimorbidity. This knowledge could be used in developing, evaluating and implementing interventions aimed at improving outcomes in T2DM patients with multimorbidity.

Methods

Study location, study design, data source and study period

We conducted the study in a tertiary care department in Ningbo, China - Department of Endocrinology and Metabolism, Ningbo First Hospital. This tertiary care hospital is responsible for the delivery of specialist healthcare services and for medical education and research.[14 15] Local people and people from surrounding areas can visit this hospital as no referral is required from the general practitioner.[14] An existing computerised medical records database was used for conducting this cross-sectional

study. The database contains information on all inpatients. Data are entered by the medico-nursing team. The quality check of the data and the overall database management are the responsibility of an independent group of hospital staff. All the conditions are coded using the International Classification of Diseases, 10th edition (ICD-10). This retrospective study included eight years of data, from 1 January 2012 to 31 December 2019, and information was available on 6755 patients.

Study population and study inclusion and exclusion criteria

Adult patients (≥18 years) with T2DM were included. If a patient was admitted more than once during the study period, data pertinent to the last admission were extracted to obtain the most up to date information on chronic conditions. Individuals with gestational diabetes, type 1 diabetes, secondary diabetes and unknown type of diabetes were excluded.

Study variables

We extracted and categorised the following information from the database:

- age (18-39 years, 40-59 years or ≥60 years),
- sex (male or female),
- education (university/college, class 7-12, class 1-6 or no qualification),
- occupation (manual worker (i.e., more physical work than mental work), non-manual worker (i.e., more mental work than physical work) or never worked/retired),
- marital status (married or single/divorced/widowed),
- residence (urban or rural using the “hukou” system (i.e., the Chinese household registration system)),
- health insurance,
- smoking (current status),
- alcohol drinking (current status),
- duration of T2DM (≤1 year, >1-5 years, >5-10 years or >10 years),

- blood glucose level (glycated haemoglobin (HbA1c <7% (good) or ≥7% (poor)), estimated using the high-performance liquid chromatographic (HPLC) method and D-10 Hemoglobin Analyzer (Bio-Rad, USA)).

In addition, information on multimorbidity was extracted. Multimorbidity was defined as having T2DM and at least one other chronic condition, each one was either a physical non-communicable disease of long duration (≥3 months), a mental health condition of long duration (≥3 months) or an infectious disease of long duration (≥3 months).[16 17] In our study, a T2DM specific complication, such as diabetic neuropathy, diabetic nephropathy, diabetic retinopathy or diabetic foot, was not counted as a chronic condition in multimorbidity. This is because these microvascular complications are in relation to the index disease (i.e., T2DM).[18 19]

Ethics

The Research Ethics Committee of Ningbo First Hospital, China approved the study (2020-R106).

Patient and public involvement

Patient and public were not involved in the study.

Statistical analyses

We calculated numbers and percentages for categorical variables and means and standard deviations (SDs) for normally distributed continuous variables. We used simple logistic regression method to investigate the association between different variables and multimorbidity. We developed a multiple logistic regression model to find any independent association. For this, we used the backward stepwise regression analysis and included all the variables. Additionally, we did a sensitivity analysis - in the multiple logistic regression model, we included only those variables that had a p-value of ≤0.20 in simple logistic regressions. We calculated odds ratios (ORs) and 95% confidence intervals (CIs). We used IBM SPSS Statistics version 26.0 for Windows for statistical analyses.

Results

4777 patients satisfied the eligibility criteria. The mean (±SD) age of patients was 64.2 (±14.2) years and around 52% (n=2482) of them were male. Over eight years, the prevalence of multimorbidity among patients with T2DM was 93.7%. The year-wise (from 2012 to 2019) prevalence was 96.9%, 95.0%, 92.9%, 95.5%, 93.2%, 91.5%, 94.0% and 93.6%, respectively.

Figure 1 shows the number of other chronic conditions in our study (in addition to T2DM). Those who had multimorbidity, the mean (±SD) number of other chronic conditions was 3 (±1). 55.6% of patients had ≥3 other chronic conditions. Table 1 reports the most common other chronic conditions in our study (in addition to T2DM). Essential hypertension (49.4%), disorders of lipoprotein metabolism and other lipidaemias (33.7%), nontoxic thyroid nodule (22.8%), fatty change of liver (20.6%) and cataract (10.7%) were the five most prevalent chronic conditions.

Table 2 reports the characteristics of the study participants. We found that multimorbidity was associated with age, sex, education, occupation, marital status, residence, health insurance and duration of T2DM. Table 3 reports the multiple backward stepwise logistic regression analysis for determining factors independently associated with multimorbidity. The odds of multimorbidity increased with the age of patients (18-39 years: 1; 40-59 years: OR 2.80, 95% CI 1.97-3.96; and ≥60 years: 6.04, 4.21-8.67). The odds were lower in female patients (0.63, 0.49-0.81), patients residing in rural areas (0.74, 0.58-0.94) and patients without health insurance (0.59, 0.43-0.80). The odds were higher in single/divorced/widowed patients compared to married patients (2.11, 1.32-3.37). In the sensitivity analysis, we found the same results.

Discussion

In our tertiary care department in Ningbo, China, around 94% of patients with T2DM had multimorbidity. We could not find any similar study conducted among patients with

T2DM in China, but in two other studies conducted among community-dwelling and hospitalised older adults, the prevalence of multimorbidity was around 49% and 69%, respectively.[20 21] This could be due to the difference in the population characteristics and the way chronic conditions were measured. Several studies have been conducted on this topic in high-income countries like the United States and in Europe.[22-26] All these studies, including our study, have highlighted the fact that multimorbidity is high among patients with T2DM.[22-26] In our study, those who had multimorbidity, the average number of other chronic conditions was three. Around 56% of patients had ≥3 other chronic conditions, and this is similar to what other studies have found.[22 23] A systematic review and meta-analysis summarising the prevalence and associated factors of multimorbidity in different geographical locations will be helpful.

In our study, essential hypertension, disorders of lipoprotein metabolism and other lipidaemias, nontoxic thyroid nodule, fatty change of liver and cataract were the five most prevalent chronic conditions. The overall profile is similar to what other studies have found.[23,24] The pathophysiological connection between T2DM and cardiovascular diseases is well known.[27 28] Similarly, T2DM and thyroid diseases are the two most common chronic conditions of the endocrine system, and patients with T2DM are more likely to develop thyroid nodule, which could be due to insulin resistance.[29 30] In our population and setting, around 72% of patients with T2DM were prescribed polypharmacy.[31] A specific medicine may be used for managing a chronic condition and the same may be contraindicated in another chronic condition. This needs to be taken into consideration when managing multimorbidity among patients with T2DM.[32] This point is valid even for preventing new chronic conditions like cardiovascular diseases among patients with T2DM. For example, the usage of a new generation of hypoglycaemic medicines, such as glucagon-like peptide 1 (GLP-1) receptor agonists and sodium-glucose cotransporter-2 (SGLT-2) inhibitors, reduces the risk of cardiovascular diseases.[33 34]

We found that the odds of multimorbidity increased with the age of patients. Age is one of the most well studied and consistent determinants of multimorbidity.[12 35] Age-related organ degeneration is a natural process and can bring in many chronic conditions.[36] However, it should be noted that multimorbidity is not equal to ageing and limited to older age alone.[37] In our study, the prevalence of multimorbidity was around 80% and 91% in the 18-39 and 40-59 years age groups, respectively. We found that the odds of multimorbidity were lower in females than in males. The finding is consistent with other studies.[22 25] This could be due to the differences at the biological level. Another potential reason could be reporting differences in sex-specific chronic conditions. For example, female patients with T2DM often present atypical symptoms of cardiovascular diseases.[38] Even the standard non-invasive diagnostic tests perform better in men than in women.[39] All these hinder the diagnosis of cardiovascular diseases in women. Another example is benign prostatic hyperplasia, which was one of the most common chronic conditions in our study. This chronic condition was diagnosed because of the compulsory ultrasound scan of the urinary system of patients with T2DM at our hospital for possible kidney comorbidities. In comparison, the gynaecological examination is not a routine examination in women with T2DM.

We found that the odds of multimorbidity were lower in patients residing in rural areas compared to urban areas. The finding is consistent with other studies.[40 41] This could be due to the economic growth, urbanisation and its negative consequences like unhealthy lifestyle.[42-44] The link between an unhealthy lifestyle and chronic conditions (particularly non-communicable diseases) is well established.[45] A similar association with multimorbidity has also emerged.[46] The other reason could be – rural patients in China have limited access to healthcare and thus, may undergo fewer diagnostic tests and confirmation of chronic conditions.[47]

We found that the odds of multimorbidity were lower in patients without health insurance compared to those with health insurance. This could be due to the fact that over 90% of the Chinese population have some sort of health insurance[48] and these

patients may undergo more diagnostic tests (within the scope of their health insurance policy) and confirmation of chronic conditions.[49] We found that the odds of multimorbidity were higher in single/divorced/widowed patients compared to married patients. The finding is consistent with other studies.[50 51] In general, the spouse of a married patient looks after them, both physically and mentally, and this could help them in managing their existing chronic conditions and preventing new chronic conditions to develop.[52 53]

Apart from the already mentioned strengths and weaknesses, the study has some more strengths and weaknesses. Multimorbidity is a less explored area in China, and to the best of our knowledge, this was the first study to explore multimorbidity among patients with T2DM in Ningbo and in the broader Zhejiang Province and China. Unlike other studies which included only older adults,[20 21 51] we included adults without any age restriction. It should be noted that multimorbidity is not equal to ageing and limited to older age alone.[37] Unlike other studies where chronic conditions in multimorbidity were self-reported by patients using a predetermined list of selected chronic conditions,[20 24] we used a holistic approach. In the database, all the conditions are coded using the International Classification of Diseases, 10th edition (ICD-10), and we included all the chronic conditions in our study. This also minimised the possibility of recall bias in our study. Our study had extremely low missing data and the multiple logistic regression analysis included a sample with missing data for the adjusted variable. Being a cross-sectional study, the causal relationship between variables and multimorbidity could not be determined. We propose conducting a longitudinal study to explore the effect of various factors on multimorbidity, including factors considered in this study and some other factors like physical activity and diet that are not present in our database and could not be adjusted for in the models. Our study had the usual routinely collected data issues as an existing medical records database was used – its main purpose is medical management and not research. The findings of our hospital-based study could be valid in similar populations and settings. We suggest conducting a population-based study that might show a distinct picture of the issue.

In conclusion, we found that a large percentage of patients with T2DM in the tertiary care department in Ningbo, China had multimorbidity and identified the associated factors. The findings could be used in developing, evaluating and implementing interventions aimed at improving outcomes in T2DM patients with multimorbidity.

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Contributors JL and KC designed the study. XL and KC analysed the data and wrote the first draft of the manuscript. SX and YC contributed to patient registration and data entry. XL contributed to data cleaning. XL, KC, SX, YC, MX, LL and JL revised it critically for important intellectual content and approved the final version.

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Competing interests None declared.

Ethics approval The Research Ethics Committee of Ningbo First Hospital, China approved the study (2020-R106).

Data sharing statement The dataset will be available upon request unless there are legal or ethical reasons for not doing so.

References

1.Health and Family Planning Commission of Ningbo Municipality. Prevention and treatment of chronic diseases in Ningbo. http://www.cnnb.com.cn/nbzfxwfbh/system/2014/05/22/008068694.shtml (accessed 25 Apr 2020).

2.Yao DZ, Sun XH, Li JH. Prevalence and risk factors of diabetes in people over 40 years of age in Ningbo city area. *Modern Practical Medicine* 2016;28:1343-45.

3.Australian Bureau of Statistics. *National Health Survey: First Result, 2014-15.* Canberra: Australian, 2015.

4.World Health Organization. *Multimorbidity*. Geneva: Switzerland, 2016.

5. Abegunde DO, Mathers CD, Adam T, *et al*. The Burden and costs of chronic diseases in low-income and middle-income countries. *Lancet* 2007; 8;370:1929-38.

6. Arokiasamy P, Uttamacharya U, Jain K, *et al*. The Impact of multimorbidity on adult physical and mental health in low- and middle-income countries: what does the study on global ageing and adult health (SAGE) reveal? *BMC Med* 2015;13:178.

7. Wei MY, Mukamal KJ. Multimorbidity, mortality, and long-term physical functioning in 3 prospective cohorts of community-dwelling adults. *Am J Epidemiol* 2018; 187:103-12.

8. Stubbs B, Vancampfort D, Veronese N, *et al*. Multimorbidity and perceived stress: a population-based cross-sectional study among older adults across six low- and middle-income countries. *Maturitas* 2018;107:84-91.

9. Ryan A, Wallace E, O'Hara P, *et al*. Multimorbidity and functional decline in community-dwelling adults: a systematic review. *Health Qual Life Outcomes* 2015;13:168.

10. Lee JT, Hamid F, Pati S, *et al*. Impact of noncommunicable disease multimorbidity on healthcare utilisation and out-of-pocket expenditures in middle-income countries: cross sectional analysis. *PLoS One* 2015;10:e0127199.

11. Paddison CA, Saunders CL, Abel GA, *et al*. Why do patients with multimorbidity in England report worse experiences in primary care? evidence from the general practice patient survey. *BMJ Open* 2015;5:e006172.

12. Palladino R, Lee JT, Ashworth M, *et al*. Associations between multimorbidity, healthcare utilisation and health status: evidence from 16 European countries. *Age Ageing* 2016;45:431-5.

13. Ubalde-Lopez M, Delclos GL, Benavides FG, *et al*. Measuring multimorbidity in a working population: the effect on incident sickness absence. *Int Arch Occup Environ Health* 2016;89:667-78.

14. Ningbo First Hospital. Hospital Introduction. http://www.nbdyyy.com/col/col100/index.html (accessed 25 Apr 2020).

15. Ministry of Health of the People's Republic of China. *The measures for the administration of the hospital grade*. Beijing: Ministry of Health of the People's Republic of China, 1989.

16. The Academy of Medical Sciences. Multimorbidity: a priority for global health research (2018). https://acmedsci.ac.uk/policy/policy-projects/multimorbidity (accessed 25 Apr 2020).

17. Bernell S, Howard SW. Use your words carefully: what is a chronic disease? *Front Public Health* 2016;4:159.

18. Radner H, Yoshida K, Smolen JS, et al. Multimorbidity and rheumatic conditions-enhancing the concept of comorbidity. *Nat Rev Rheumatol* 2014;10:252-6.

19. Valderas JM, Starfield B, Sibbald B, *et al*. Defining comorbidity: implications for understanding health and health services. *Ann Fam Med* 2009;7:357-63.

20. Gu J, Chao J, Chen W, *et al*. Multimorbidity in the community-dwelling elderly in urban China. *Arch Gerontol Geriatr* 2017;68:62-7.

21. Zhang L, Ma L, Sun F, *et al*. A multicenter study of multimorbidity in older adult inpatients in China. *J Nutr Health Aging* 2020;24:269-76.

22. Alonso-Morán E, Orueta JF, Esteban JI, *et al*. Multimorbidity in people with type 2 diabetes in the Basque country (Spain): prevalence, comorbidity clusters and comparison with other chronic patients. *Eur J Intern Med* 2015;26:197-202.

23. Lin PJ, Kent DM, Winn A, *et al*. Multiple chronic conditions in type 2 diabetes mellitus: prevalence and consequences. *Am J Manag Care* 2015;21:e23-34.

24. Teljeur C, Smith SM, Paul G, *et al*. Multimorbidity in a cohort of patients with type 2 diabetes. *Eur J Gen Pract* 2013;19:17-22.

25. Iglay K, Hannachi H, Howie PJ, *et al*. Prevalence and co-prevalence of comorbidities among patients with type 2 diabetes mellitus. *Curr Med Res Opin* 2016;32:1243-52.

26. Hermans MP, Dath N. Prevalence and co-prevalence of comorbidities in Belgian patients with type 2 diabetes mellitus: a transversal, descriptive study. *Acta Clin Belg* 2018;73:68-74.

27. Laakso M, Kuusisto J. Insulin resistance and hyperglycaemia in cardiovascular disease development. *Nat Rev Endocrinol* 2014;10:293-302.

28. Henning RJ. Type-2 diabetes mellitus and cardiovascular disease. *Future Cardiol* 2018;14:491-509.

29. Tang Y, Yan T, Wang G, *et al*. Correlation between insulin resistance and thyroid nodule in type 2 diabetes mellitus. *Int J Endocrinol* 2017;2017:1617458.

30. Zhang HM, Feng QW, Niu YX, *et al*. Thyroid nodules in type 2 diabetes mellitus. *Curr Med Sci* 2019;39:576-81.

31. Li J, Chattopadhyay K, Xu M, *et al*. Prevalence and predictors of polypharmacy prescription among type 2 diabetes patients at a tertiary care department in Ningbo, China: a retrospective database study. *PLoS One* 2019;14:e0220047.

32. Marengoni A, Onder G. Guidelines, polypharmacy, and drug-drug interactions in patients with multimorbidity. *BMJ* 2015;350:h1059.

33. Zelniker TA, Wiviott SD, Raz I, *et al*. SGLT2 inhibitors for primary and secondary prevention of cardiovascular and renal outcomes in type 2 diabetes: a systematic review and meta-analysis of cardiovascular outcome trials. *Lancet* 2019;393:31-9.

34. Bethel MA, Patel RA, Merrill P, *et al*. Cardiovascular outcomes with glucagon-like peptide-1 receptor agonists in patients with type 2 diabetes: a meta-analysis. *Lancet Diabetes Endocrinol* 2018;6:105-13.

35. Afshar S, Roderick PJ, Kowal P, *et al*. Multimorbidity and the inequalities of global ageing: a cross-sectional study of 28 countries using the world health surveys. *BMC Public Health* 2015;15:776.

36. King M, Lipsky MS. Clinical implications of aging. *Dis Mon* 2015;61:467-74.

37. van Oostrom SH, Gijsen R, Stirbu I, *et al*. Time trends in prevalence of chronic diseases and multimorbidity not only due to aging: data from general practices and health surveys. *PLoS One* 2016;11:e0160264.

38. Wada H, Miyauchi K, Daida H. Gender Differences in the clinical features and outcomes of patients with coronary artery disease. *Expert Rev Cardiovasc Ther* 2019;17:127-33.

39. Shah AS, Griffiths M, Lee KK, *et al*. High sensitivity cardiac troponin and the under-diagnosis of myocardial infarction in women: prospective cohort study. *BMJ* 2015;350:g7873.

40. Yi JY, Kim H, Chi I. Urban-rural differences in multimorbidity and associated factors in China and Korea: a population-based survey study. *Geriatr Gerontol Int* 2019;19:1157-64.

41. Yao SS, Cao GY, Han L, *et al*. Prevalence and patterns of multimorbidity in a nationally representative sample of older Chinese: results from CHARLS. *J Gerontol A Biol Sci Med Sci* 2019;glz185.

42. Zhu W, Chi A, Sun Y. Physical activity among older Chinese adults living in urban and rural areas: a review. *J Sport Health Sci* 2016;5:281-6.

43. Muntner P, Gu D, Wildman RP, *et al*. Prevalence of physical activity among Chinese adults: results from the international collaborative study of cardiovascular disease in Asia. *Am J Public Health* 2005;95:1631-6.

44. Miao J, Wu X. Urbanization, socioeconomic status and health disparity in China. *Health Place* 2016;42:87-95.

45. World Health Organization. *Global action plan for the prevention and control of NCD 2013-2020*. Geneva: Switzerland, 2013.

46. Vancampfort D, Koyanagi A, Ward PB, *et al*. Chronic physical conditions, multimorbidity and physical activity across 46 low- and middle-income countries. *Int J Behav Nutr Phys Act* 2017;14:6.

47. Liu Z, Albanese E, Li S, *et al*. Chronic disease prevalence and care among the elderly in urban and rural Beijing, China - a 10/66 dementia research group cross-sectional survey. *BMC Public Health* 2009;9:394.

48. Zhao C, Wang C, Shen C, *et al*. China's achievements and challenges in improving health insurance coverage. *Drug Discov Ther* 2018;12:1-6.

49. Yang C, Huang Z, Sun K, *et al*. Comparing the economic burden of type 2 diabetes mellitus patients with and without medical insurance: a cross-sectional study in China. *Med Sci Monit* 2018;24:3039-102.

50. Park B, Ock M, Lee HA, *et al*. Multimorbidity and health-related quality of life in Koreans aged 50 or older using KNHANES 2013-2014. *Health Qual Life Outcomes* 2018;16:186.

51. Aminisani N, Stephens C, Allen J, *et al*. Socio-demographic and lifestyle factors associated with multimorbidity in New Zealand. *Epidemiol Health* 2020;42:e2020001.

52. Stroebe M, Schut H, Stroebe W. Health outcomes of bereavement. *Lancet* 2007; 370:1960-73.

53. Parajuli J, Saleh F, Thapa N, Ali L. Factors associated with nonadherence to diet and physical activity among Nepalese type 2 diabetes patients: a cross sectional study. *BMC Res Notes* 2014;7:758.

Figure 1. Number of other chronic conditions in our study (in addition to T2DM).

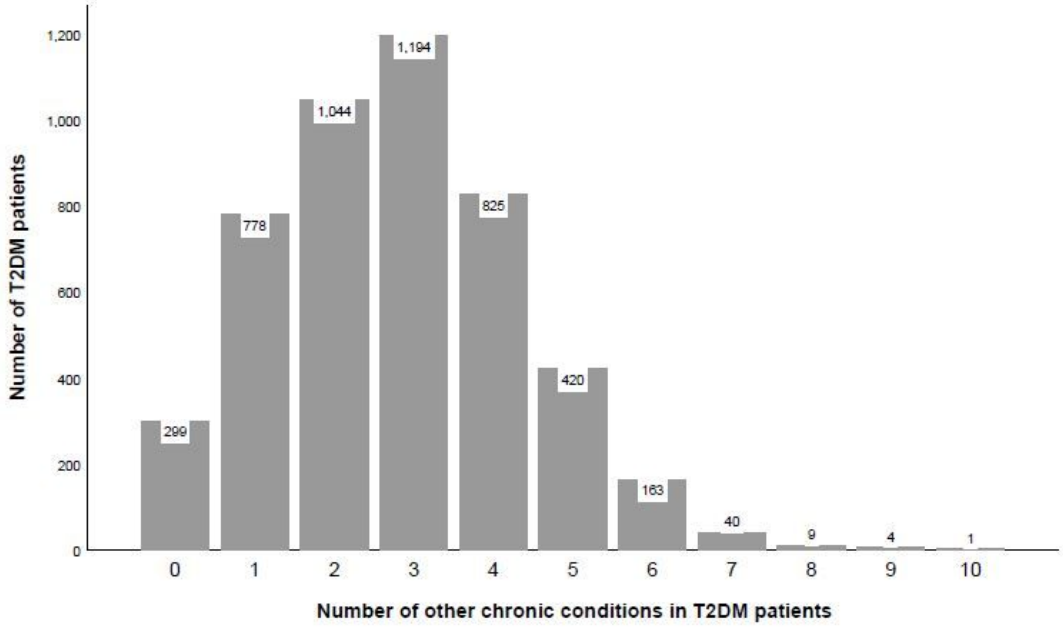

Table 1. Most common other chronic conditions in our study (in addition to T2DM).

Most common other chronic conditions (based on ICD-10 classification)	Patients with T2DM n (%)
Essential hypertension (I10)	2362 (49.4)
Disorders of lipoprotein metabolism and other lipidaemias (E78)	1612 (33.7)
Nontoxic thyroid nodule (E04)	1088 (22.8)
Fatty (change of) liver (K76)	984 (20.6)
Cataract (H26)	512 (10.7)
Chronic ischemic heart disease (I25)	455 (9.5)
Atherosclerosis (I70)	411 (8.6)
Osteoporosis (M81)	348 (7.3)
Cerebral infarction (I63)	341 (7.1)
Benign prostatic hyperplasia (N40)	303 (12.2*)

Abnormal findings on diagnostic imaging of lung (R91)	287 (6.0)
Thoracic, thoracolumbar, and lumbosacral intervertebral disc disorders (M51)	260 (5.4)
Obesity (E66)	177 (3.7)
Cervical disc disorders (M50)	161 (3.4)
Chronic viral hepatitis (B18)	138 (2.9)
Sleep disorders (G47)	135 (2.8)
Gout (M10)	132 (2.8)
Disorders of purine and pyrimidine metabolism (E79)	127 (2.7)
Atrial fibrillation and flutter (I48)	118 (2.5)
Gastro-esophageal reflux disease (K21)	111 (2.3)

*In 2482 males.

Table 2. Characteristics of the study participants.

	Total (4777)	**Multimorbidity No (299) n (%)**	**Multimorbidity Yes (4478) n (%)**	**Unadjusted OR (95% CI)**	**P value**
Age (years)					<0.001
18-39	308	63 (20.5)	245 (79.5)	1	
40-59	1360	120 (8.8)	1240 (91.2)	2.66 (1.90,3.71)	
≥60	3109	116 (3.7)	2993 (96.3)	6.64 (4.75,9.26)	
Sex					0.008
Male	2482	133 (5.4)	2349 (94.6)	1	
Female	2295	166 (7.2)	2129 (92.8)	0.73 (0.57,0.92)	
Education					0.005
University/college	545	47 (8.6)	498 (91.4)	1	
Class 7-12	1927	136 (7.1)	1791 (92.9)	1.24 (0.88,1.76)	
Class 1-6	1574	80 (5.1)	1494 (94.9)	1.76 (1.21,2.56)	
No qualification	731	36 (4.9)	695 (95.1)	1.82 (1.16,2.86)	
Occupation					<0.001
Manual worker	1088	74 (6.8)	1014 (93.2)	1	
Non-manual worker	1884	152 (8.1)	1732 (91.9)	0.83 (0.62,1.10)	
Never worked/retired	1805	73 (4.0)	1732 (96.0)	1.73 (1.24,2.41)	
Marital status					0.008
Married	4207	278 (6.6)	3929 (93.4)	1	
Single/divorced/widowed	570	21 (3.7)	549 (96.3)	1.85 (1.18,2.91)	
Residence					<0.001
Urban	2815	145 (5.2)	2670 (94.8)	1	
Rural	1962	154 (7.8)	1808 (92.2)	0.64 (0.50,0.81)	
Health insurance					<0.001
Yes	4211	232 (5.5)	3979 (94.5)	1	
No	564	67 (11.9)	497 (88.1)	0.43 (0.33,0.58)	
Smoking (current status)					0.073
No	3714	245 (6.6)	3469 (93.4)	1	

Yes	1063	54 (5.1)	1009 (94.9)	1.32 (0.98,1.79)	
Alcohol drinking (current status)					0.713
No	4169	263 (6.3)	3906 (93.7)	1	
Yes	608	36 (5.9)	572 (94.1)	1.07 (0.75,1.53)	
Duration of T2DM (years)					<0.001
≤1	981	93 (9.5)	888 (90.5)	1	
>1-5	880	60 (6.8)	820 (93.2)	1.43 (1.02,2.01)	
>5-10	1247	74 (5.9)	1173 (94.1)	1.66 (1.21,2.28)	
>10	1669	72 (4.3)	1597 (95.7)	2.32 (1.69,3.19)	
Blood glucose level (HbA1c)					0.458
<7%	899	64 (7.1)	835 (92.9)	1	
≥7%	3748	226 (6.0)	3522 (94.0)	1.19 (0.90,1.59)	
Unknown	130	9 (6.9)	121 (93.1)	1.03 (0.50,2.12)	

Table 3. Multiple backward stepwise logistic regression analysis for determining factors independently associated with multimorbidity.

	Adjusted OR (95% CI)	P value
Age (years)		<0.001
18-39	1	
40-59	2.80 (1.97,3.96)	
≥60	6.04 (4.21,8.67)	
Sex		<0.001
Male	1	
Female	0.63 (0.49,0.81)	
Marital status		0.002
Married	1	
Single/divorced/widowed	2.11 (1.32,3.37)	
Residence		0.014
Urban	1	
Rural	0.74 (0.58,0.94)	
Health insurance		<0.001
Yes	1	
No	0.59 (0.43,0.80)	

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1,2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2,3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4,5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4,5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5,6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5,6
Bias	9	Describe any efforts to address potential sources of bias	5,6
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5,6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	n/a
		(*c*) Explain how missing data were addressed	6, Table2
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	n/a
		(*e*) Describe any sensitivity analyses	6
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5,7
		(b) Give reasons for non-participation at each stage	n/a
		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7, Table2
		(b) Indicate number of participants with missing data for each variable of interest	Table2
Outcome data	15*	Report numbers of outcome events or summary measures	7, Figure 1, Table1, Table2
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7, Table2
		(*b*) Report category boundaries when continuous variables were categorized	7, Table2, Table3
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	7
Discussion			
Key results	18	Summarise key results with reference to study objectives	7,8,9,10
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	7,8,9,10
Generalisability	21	Discuss the generalisability (external validity) of the study results	10
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	11

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Prevalence of comorbidities and their associated factors in patients with type 2 diabetes at a tertiary care department in Ningbo, China: a cross-sectional study

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Title

Prevalence of comorbidities and their associated factors in patients with type 2 diabetes at a tertiary care department in Ningbo, China: a cross-sectional study

Xueyu Li*[1, 2], Kaushik Chattopadhyay*[3], Shengnan Xu[2], Yanshu Chen[2], Miao Xu[2], Li Li[2], Jialin Li[2]

[1]Ningbo University Medical School, Ningbo, PR China

[2]Department of Endocrinology and Metabolism, Ningbo First Hospital, Ningbo, PR China

[3]Division of Epidemiology and Public Health, School of Medicine, University of Nottingham, Nottingham, UK

*These authors contributed equally to this work.

Corresponding author: Dr Jialin Li, e-mail; lijialin@sina.com

Abstract

Objectives To determine the prevalence of comorbidities in patients with type 2 diabetes (T2DM) and identify the factors independently associated with comorbidities in a tertiary care department in Ningbo, China.

Design A computerised medical records database was used to conduct a cross-sectional study.

Setting The study was conducted in a tertiary care department in Ningbo, China.

Participants The study was conducted on adult patients with T2DM, and it included eight years of data, from 1 January 2012 to 31 December 2019.

The primary outcome measure Comorbidity was defined as the co-existence of at least one other chronic condition, i.e., either a physical non-communicable disease (duration ≥3 months), a mental health condition (duration ≥3 months), or an infectious disease (duration ≥3 months).

Results In total, 4777 patients with T2DM satisfied the eligibility criteria. Over eight years, the prevalence of comorbidities was 93.7%. The odds of comorbidities increased with the age of patients (18–39 years: 1; 40–59 years: odds ratio 2.80, 95% confidence interval 1.98–3.96; 60–69 years: 4.43, 3.04–6.44; and ≥70 years: 10.97, 7.17–16.77). The odds were lower in female patients (0.66, 0.51–0.84), patients residing in rural areas (0.75, 0.59–0.95), and patients without health insurance (0.62, 0.46–0.83). The odds were higher in single/divorced/widowed patients compared to those in married patients (1.95, 1.21–3.12).

Conclusions A large percentage of patients with T2DM in the tertiary care department in Ningbo, China, had comorbidities, and the factors associated with comorbidities were identified. The findings could be used in developing, evaluating, and

implementing interventions aimed at improving outcomes in patients with T2DM with comorbidities.

Keywords

comorbidity, type 2 diabetes, China

Strengths and limitations of the study

Ours was the first study to investigate comorbidities in patients with type 2 diabetes in Ningbo and the broader Zhejiang Province of China.

We included all the chronic conditions in our study; they were coded using the International Classification of Diseases, 10th edition (ICD-10) in our database.

Our study had extremely low missing data and the multiple logistic regression analysis included a sample with missing data for the adjusted variable.

As it was a cross-sectional study, the causal relationship between the variables and the comorbidities could not be determined.

The high prevalence of comorbidities in our study could be due to the study setting (i.e., hospital).

INTRODUCTION

Ningbo is an economically developed Chinese city in Zhejiang Province. The population of the city is approximately 8.2 million.[1] Non-communicable diseases, mental health conditions, and infectious diseases are prevalent in the city.[2] Of these, one of the most prevalent non-communicable diseases is type 2 diabetes (T2DM). T2DM is a chronic complex metabolic disorder. China has the largest T2DM epidemic in the world, and in Ningbo, its prevalence in adults ⩾ 40 years of age is 21%.[3] In Ningbo, the diabetes-related mortality is 14.5 per 100,000 population.[4]

There is no international consensus regarding the best way to define comorbidity. It is usually defined as the co-existence of other conditions with an index condition (i.e., the main condition under study) where these other conditions are not consequences of the index condition.[5-7] Comorbidities accelerate the progression of individual conditions, encourage the development of other physical and mental conditions, and even lead to premature mortality.[8-10] Moreover, they negatively affect overall health, wellbeing, and functioning.[11, 12] Additionally, they lead to high treatment burden, high healthcare utilisation and expenditure, and loss of economic output.[13, 14] In real life, T2DM is rarely presented in isolation and is always accompanied by comorbidity.[15, 16]

To date, no study has been undertaken to investigate comorbidities in patients with T2DM in Ningbo. The study objectives were to determine the prevalence of comorbidities in patients with T2DM and identify the factors independently associated with comorbidities. This knowledge could be used in developing, evaluating, and implementing interventions aimed at improving outcomes in patients with T2DM with comorbidities.

METHODS

Study location, study design, data source, and study period

We conducted the study in a tertiary care department, the Department of Endocrinology and Metabolism, Ningbo First Hospital, in Ningbo, China. This tertiary care hospital delivers speciality healthcare services, provides medical education, and conducts research.[17,18] Locals and people from the surrounding areas visit this hospital as no referral is required from the general practitioner.[17] An existing computerised medical records database was used for conducting this cross-sectional study. This database contained information on all inpatients. Since it was a real-time database, new patients were added continuously. Data were entered by the medico-nursing team and an independent group of the hospital staff was responsible for assessing the quality of the data and overall database management. All the conditions were coded using the International Classification of Diseases, 10th edition (ICD-10). This retrospective study included eight years of data, from 1 January 2012 to 31 December 2019, and the information was available on 6755 patients.

Study population and study inclusion and exclusion criteria

Adult patients (≥ 18 years) with T2DM were included. If a patient was admitted more than once during the study period, data pertinent to the last admission were extracted to obtain the most recent information on health conditions. Individuals with gestational diabetes, type 1 diabetes, secondary diabetes, and unknown types of diabetes were excluded.

Study variables

We extracted and categorised the following information from the database:

- age (18–39 years, 40–59 years, 60–69 years or ≥70 years),
- sex (male or female),
- education (university/college, class 7–12, class 1–6, or no qualification),

- occupation (manual worker [i.e., more physical work than mental work], non-manual worker [i.e., more mental work than physical work], or never worked/retired),
- marital status (married or single/divorced/widowed),
- residence (urban or rural using the "hukou" system i.e., the Chinese household registration system),
- health insurance,
- smoking (current status),
- alcohol consumption (current status),
- duration of T2DM (≤ 1 year, > 1–5 years, > 5–10 years, or > 10 years), and
- blood glucose level (glycated haemoglobin [HbA1c < 7% (good) or ≥ 7% (poor)], estimated using the high-performance liquid chromatographic method and D-10 Haemoglobin Analyser [Bio-Rad, USA]). In China, the recommended HbA1c treatment target did not change over the study period (< 7% for most patients with T2DM).[19-21]

In addition, information on comorbidities was extracted. The index condition was T2DM. Comorbidity was defined as the co-existence of at least one other chronic condition, i.e., either a physical non-communicable disease (duration ≥ 3 months), a mental health condition (duration ≥ 3 months), or an infectious disease (duration ≥ 3 months).[5-7] T2DM-specific complications (i.e., microvascular complications, such as diabetic retinopathy, nephropathy, and neuropathy/foot) were excluded as these were consequences of the index condition; hence, they were not considered as comorbidities.[6]

Ethics

The Research Ethics Committee of the Ningbo First Hospital, China, approved this study (2020-R106). The researchers had no access to information that could identify individual patients during the data analyses. No informed consent was required as per

research ethics rules.

Patient and public involvement

Patients and public were not involved in the study.

Statistical analyses

We calculated numbers and percentages for categorical variables, and means and standard deviations (SDs) for normally distributed continuous variables. We used a simple logistic regression method to investigate the association between the different variables and comorbidities. We developed a multiple logistic regression model to identify any independent associations. For this, we used backward stepwise regression analysis and included all the variables. Additionally, we performed a sensitivity analysis — in the multiple logistic regression model, we included only those variables that had a p-value ≤ 0.20 in simple logistic regressions. We calculated odds ratios (ORs) and 95% confidence intervals (CIs). We used IBM SPSS Statistics version 26.0 for Windows for statistical analyses.

RESULTS

A total of 4777 patients with T2DM satisfied the eligibility criteria. The mean (±SD) age of patients was 64.2 (±14.2) years, and approximately 52% (n=2482) of them were men. The mean (±SD) HbA1c level was 9.2% (±2.4%). Over eight years, the prevalence of comorbidities was 93.7%. The year-wise prevalences from 2012 to 2019 were 96.9%, 95.0%, 92.9%, 95.5%, 93.2%, 91.5%, 94.0%, and 93.6%, respectively.

Figure 1 shows the number of comorbidities in our study. The mean (±SD) number of comorbidities was 3 (±1). Figure 2 shows the number of comorbidities in our study in the different age groups. In the ⩾ 70 years age group, 68.5% (1247) had ⩾ 3 comorbidities, whereas the prevalences were only 33.1% (102), 43.5% (592), and 55.5% (715) in the 18–39, 40–59, and 60–69 years age groups, respectively. Table 1 reports

the most common comorbidities in our study. Essential hypertension (49.4%), disorders of lipoprotein metabolism and other lipidaemias (33.7%), nontoxic thyroid nodule (22.8%), fatty change of liver (20.6%), and cataract (10.7%) were the five most prevalent comorbidities.

Table 2 reports the characteristics of the study participants. We found that the comorbidities were associated with age, sex, education, occupation, marital status, residence, health insurance, and the duration of T2DM. Table 3 reports the multiple backward stepwise logistic regression analysis for determining factors independently associated with the comorbidities. The odds of comorbidities increased with the age of patients (18–39 years: 1; 40–59 years: OR 2.80, 95% CI 1.98–3.96; 60–69 years: 4.43, 3.04–6.44; and ≥70 years: 10.97, 7.17–16.77). The odds were lower in female patients (0.66, 0.51–0.84), patients residing in rural areas (0.75, 0.59–0.95), and patients without health insurance (0.62, 0.46–0.83). The odds were higher in single/divorced/widowed patients compared to married patients (1.95, 1.21–3.12). We obtained similar results in the sensitivity analysis.

DISCUSSION

In our tertiary care department in Ningbo, China, approximately 94% of the patients with T2DM had comorbidities and this influenced the overall management. In a previous study, we found that approximately 72% of the patients with T2DM were prescribed polypharmacy.[22] There are no similar studies on comorbidities conducted in patients with T2DM in China published in the English language. However, we found two similar studies published in Mandarin: one on patients with diabetes at a community health centre and another on outpatients with T2DM at a tertiary care hospital.[23, 24] The corresponding prevalence figures were around 95% and 73%, respectively. The different prevalence figures could be explained by the differences in population characteristics, the study setting, and the definition of comorbidity applied. Several studies have been conducted on this subject in high-income countries such as

the United States and European countries.[25-29] All these studies, and also our study, have highlighted the fact that comorbidities are highly prevalent in patients with T2DM. A systematic review and meta-analysis of the prevalence and the factors associated with comorbidities in patients with T2DM in different geographical locations will be helpful.

Comorbidities are not synonymous with complications.[6] In a previous study on the vascular complications of T2DM, we included microvascular complications (i.e., diabetic retinopathy, nephropathy, and neuropathy/foot) and macrovascular complications (i.e., coronary heart disease, stroke, and peripheral arterial disease) and found that more than half of the patients with T2DM had vascular complications.[30] In the present study, we explored comorbidities in patients with T2DM using a recommended definition. Comorbidity was defined as the co-existence of at least one other chronic condition, either a physical (non-communicable/infectious disease) or mental health condition.[5-7] Unlike the previous study, in the present study, microvascular complications were excluded, as these were consequences of T2DM and should not be considered as comorbidities.[6]

We found that the odds of comorbidities increased with age in patients with T2DM. Age is one of the most well-studied and consistent determinants of comorbidities.[25, 28, 31] Age-related organ degeneration is a natural process and can lead to the development of many health conditions.[32] However, it should be noted that comorbidities do not correspond with age and they are not limited to the older population alone.[33] In our study, the prevalences of comorbidities were around 80% and 91% in the 18–39 and 40–59 years age groups, respectively. We found that the odds of comorbidities were lower in female patients with T2DM compared with those in their male counterparts. This finding is consistent with other studies.[25, 28] This could be due to differences at the biological level. Another potential reason could be the reporting differences in sex-specific health conditions. For example, female patients with T2DM often present with atypical symptoms of cardiovascular

diseases.[34] Additionally, the standard non-invasive diagnostic tests perform better in men than in women.[35] All these hinder the diagnosis of cardiovascular diseases in women. Another example is benign prostatic hyperplasia, one of the most common comorbidities in our study. This comorbidity was diagnosed because of the compulsory ultrasound scan of the urinary system of patients with T2DM at our hospital for possible kidney diseases. In comparison, the gynaecological examination is not a routine examination in women with T2DM.

We found that the odds of comorbidities were lower in patients with T2DM residing in rural areas compared to those in urban areas. This could be due to economic growth, urbanisation, and its negative consequences such as an unhealthy lifestyle.[36-38] The link between an unhealthy lifestyle and chronic conditions (particularly non-communicable diseases) is well established.[39] A similar association has also emerged with comorbidities.[23, 40] Another reason could be that rural patients in China have limited access to healthcare and thus, they may undergo fewer diagnostic tests and obtain fewer confirmations of health conditions.[41] We found that the odds of comorbidities were lower in patients with T2DM without health insurance compared to those with health insurance. This could be due to the fact that over 90% of the Chinese population have some sort of health insurance,[42] and these patients may undergo more diagnostic tests (within the scope of their health insurance policy) and obtain confirmation of a range of health conditions.[43] We found that the odds of comorbidities were higher in single/divorced/widowed patients with T2DM compared with those in married patients. In general, the spouses of married patients provide both physical and mental support to them, and this could help them manage their existing health conditions and prevent new ones from emerging.[44,45]

This study has several strengths and weaknesses. Comorbidity is a less-explored area in China, and to the best of our knowledge, this was the first study to explore comorbidities in patients with T2DM in Ningbo and the broader Zhejiang Province. The quality of our routinely collected data was good. Unlike other studies where

comorbidities in T2DM were self-reported by the patients with T2DM using a predetermined list of selected comorbidities,[23, 24] we used a holistic approach. All the conditions were coded using the International Classification of Diseases, 10th edition (ICD-10) in our database, and we included all the chronic conditions in our study. This also minimised the possibility of recall bias in our study. Our study had extremely low missing data; only HbA1c data were missing in 130 patients out of 4777 (i.e., 2.7%). Multiple logistic regression analysis included a sample with missing data for the adjusted variable. Since it was a cross-sectional study, the causal relationship between variables and comorbidities could not be determined. We propose to conduct a longitudinal study to explore the effects of various factors on comorbidities, including factors considered in this study and other factors such as physical activity and diet that were not present in our database and could not be adjusted for in the models. In our study, the high prevalence of comorbidities could be due to the study setting (i.e., hospital). The findings of our hospital-based study could be valid in similar settings. We suggest conducting a population-based study that might provide a distinct picture of the issue in Ningbo.

In conclusion, we found that a large percentage of patients with T2DM in the tertiary care department in Ningbo, China, had comorbidities, and we also identified the factors associated with comorbidities. The findings could be used in developing, evaluating, and implementing interventions aimed at improving outcomes in patients with T2DM with comorbidities.

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CONTRIBUTORS JL and KC designed the study. XL and KC analysed the data and wrote the first draft of the manuscript. SX and YC contributed to patient registration and data entry. XL contributed to data cleaning. XL, KC, SX, YC, MX, LL and JL revised it critically for important intellectual content and approved the final version.

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COMPETING INTERESTS None declared.

ETHICS APPROVAL The Research Ethics Committee of Ningbo First Hospital, China approved the study (2020-R106).

DATA SHARING STATEMENT The dataset will be available upon request unless there are legal or ethical reasons for not doing so.

REFERENCES

1. Ningbo Municipal Statistics Bureau. Statistical Bulletin on National Economic and Social Development in Ningbo, China, 2018.

2. Health and Family Planning Commission of Ningbo Municipality. Prevention and treatment of chronic diseases in Ningbo. http://www.cnnb.com.cn/nbzfxwfbh/system/2014/05/22/008068694.shtml (accessed 25 Apr 2020).

3. Yao DZ, Sun XH, Li JH. Prevalence and risk factors of diabetes in people over 40 years of age in Ningbo city area. *Modern Practical Medicine* 2016;28:1343-5.

4. Li H, Cui J, Gong J, *et al*. Diabetes morbidity and mortality of residents in Ningbo, 2010-2014. *Chinese Rural Health Service Administration* 2016;36:1304-7.

5. World Health Organization. *Multimorbidity*. Geneva: Switzerland, 2016.

6. Ording AG, Sørensen HT. Concepts of comorbidities, multiple morbidities, complications, and their clinical epidemiologic analogs. *Clin Epidemiol* 2013;5:199-203.

7. Valderas JM, Starfield B, Sibbald B, *et al*. Defining comorbidity: implications for understanding health and health services. *Ann Fam Med* 2009;7:357-63.

8. Einarson TR, Acs A, Ludwig C, *et al*. Prevalence of cardiovascular disease in type 2 diabetes: a systematic literature review of scientific evidence from across the world

in 2007-2017. *Cardiovasc Diabetol* 2018;17:83.

9. Nouwen A, Winkley K, Twisk J, *et al*. Type 2 diabetes mellitus as a risk factor for the onset of depression: a systematic review and meta-analysis. *Diabetologia* 2010;53:2480-6.

10. Yokomichi H, Nagai A, Hirata M, *et al*. Survival of macrovascular disease, chronic kidney disease, chronic respiratory disease, cancer and smoking in patients with type 2 diabetes: BioBank Japan cohort. *J Epidemiol* 2017;27:S98-S106.

11. Adriaanse MC, Drewes HW, van der Heide I, *et al*. The impact of comorbid chronic conditions on quality of life in type 2 diabetes patients. *Qual Life Res* 2016;25:175-82.

12. Wermeling PR, Gorter KJ, van Stel HF, *et al*. Both cardiovascular and non-cardiovascular comorbidity are related to health status in well-controlled type 2 diabetes patients: a cross-sectional analysis. *Cardiovasc Diabetol* 2012;11:121.

13. Gruneir A, Markle-Reid M, Fisher K, *et al*. Comorbidity burden and health services use in community-living older adults with diabetes mellitus: a retrospective cohort study. *Can J Diabetes* 2016;40:35-42.

14. Terauchi Y, Ozaki A, Zhao XH, *et al*. Humanistic and economic burden of cardiovascular disease related comorbidities and hypoglycaemia among patients with type 2 diabetes in Japan. *Diabetes Res Clin Pract* 2019;149:115-25.

15. Australian Bureau of Statistics. *National Health Survey: First Result, 2014-15.* Canberra: Australian, 2015.

16. Druss BG, Marcus SC Olfson M, *et al*. Comparing the national economic burden of five chronic conditions. *Health Aff (Millwood)* 2001;20:233-41.

17. Ningbo First Hospital. Hospital Introduction. http://www.nbdyyy.com/col/col100/index.html (accessed 25 Apr 2020).

18. Ministry of Health of the People's Republic of China. *The measures for the administration of the hospital grade*. Beijing: Ministry of Health of the People's Republic of China, 1989.

19. Chinese Diabetes Society. China guideline for type 2 diabetes (2010 ed). *Chin J Diabetes* 2012;20:S1-S36.

20. Chinese Diabetes Society. China guideline for type 2 diabetes (2013 ed). *Chin J Endocrinol Metab* 2014;30:893-942.

21. Jia W, Weng J, Zhu D, *et al*. Standards of medical care for type 2 diabetes in China 2019. *Diabetes Metab Res Rev* 2019;35:e3158.

22. Li J, Chattopadhyay K, Xu M, *et al*. Prevalence and predictors of polypharmacy prescription among type 2 diabetes patients at a tertiary care department in Ningbo, China: a retrospective database study. *PLoS One* 2019;14:e0220047.

23. Xing Y, Wang P, Yang X. A survey of comorbidity and health behaviors of diabetic patients in an area of Beijing. *Journal of Chinese Physician* 2020;22:379-84.

24. Zhao W, Zhao D, Wang X, *et al*. Current status and influential factors of co-morbidity for patients with type 2 diabetes mellitus in Tongzhou district of Beijing. *Chin J Health Manage* 2019;13:541-5.

25. Alonso-Morán E, Orueta JF, Esteban JI, *et al*. Multimorbidity in people with type 2 diabetes in the Basque country (Spain): prevalence, comorbidity clusters and comparison with other chronic patients. *Eur J Intern Med* 2015;26:197-202.

26. Lin PJ, Kent DM, Winn A, *et al*. Multiple chronic conditions in type 2 diabetes mellitus: prevalence and consequences. *Am J Manag Care* 2015;21:e23-34.

27. Teljeur C, Smith SM, Paul G, *et al*. Multimorbidity in a cohort of patients with type 2 diabetes. *Eur J Gen Pract* 2013;19:17-22.

28. Iglay K, Hannachi H, Howie PJ, *et al*. Prevalence and co-prevalence of comorbidities among patients with type 2 diabetes mellitus. *Curr Med Res Opin* 2016;32:1243-52.

29. Hermans MP, Dath N. Prevalence and co-prevalence of comorbidities in Belgian patients with type 2 diabetes mellitus: a transversal, descriptive study. *Acta Clin Belg* 2018;73:68-74.

30. Li J, Chattopadhyay K, Xu M, *et al*. Prevalence and associated factors of vascular complications among inpatients with type 2 diabetes: a retrospective database study at a tertiary care department, Ningbo, China. *PloS One* 2020;15:e0235161.

31. Mata-Cases M, Franch-Nadal J, Real J, *et al*. Prevalence and coprevalence of chronic comorbid conditions in patients with type 2 diabetes in Catalonia: a population-based cross-sectional study. *BMJ Open* 2019;9:e031281.

32. King M, Lipsky MS. Clinical implications of aging. *Dis Mon* 2015;61:467-74.

33. van Oostrom SH, Gijsen R, Stirbu I, *et al*. Time trends in prevalence of chronic diseases and multimorbidity not only due to aging: data from general practices and

health surveys. *PLoS One* 2016;11:e0160264.

34. Wada H, Miyauchi K, Daida H. Gender Differences in the clinical features and outcomes of patients with coronary artery disease. *Expert Rev Cardiovasc Ther* 2019;17:127-33.

35. Shah AS, Griffiths M, Lee KK, *et al*. High sensitivity cardiac troponin and the under-diagnosis of myocardial infarction in women: prospective cohort study. *BMJ* 2015;350:g7873.

36. Zhu W, Chi A, Sun Y. Physical activity among older Chinese adults living in urban and rural areas: a review. *J Sport Health Sci* 2016;5:281-6.

37. Muntner P, Gu D, Wildman RP, *et al*. Prevalence of physical activity among Chinese adults: results from the international collaborative study of cardiovascular disease in Asia. *Am J Public Health* 2005;95:1631-6.

38. Miao J, Wu X. Urbanization, socioeconomic status and health disparity in China. *Health Place* 2016;42:87-95.

39. World Health Organization. *Global action plan for the prevention and control of NCD 2013-2020*. Geneva: Switzerland, 2013.

40. Wang X. Chen J, Liu X, *et al*. Identifying patterns of lifestyle behaviors among people with type 2 diabetes in Tianjin, China: a latent class analysis. *Diabetes Ther* 2017;8:1379-92.

41. Liu Z, Albanese E, Li S, *et al*. Chronic disease prevalence and care among the elderly in urban and rural Beijing, China - a 10/66 dementia research group cross-sectional survey. *BMC Public Health* 2009;9:394.

42. Zhao C, Wang C, Shen C, *et al*. China's achievements and challenges in improving health insurance coverage. *Drug Discov Ther* 2018;12:1-6.

43. Yang C, Huang Z, Sun K, *et al*. Comparing the economic burden of type 2 diabetes mellitus patients with and without medical insurance: a cross-sectional study in China. *Med Sci Monit* 2018;24:3039-102.

44. Stroebe M, Schut H, Stroebe W. Health outcomes of bereavement. *Lancet* 2007; 370:1960-73.

45. Parajuli J, Saleh F, Thapa N, Ali L. Factors associated with nonadherence to diet and physical activity among Nepalese type 2 diabetes patients: a cross sectional study. *BMC Res Notes* 2014;7:758.

Figure 1. Number of comorbidities in our study.

Figure 2. Number of comorbidities in our study in the different age groups.

Table 1. Most common comorbidities in our study.

Most common comorbidities (based on ICD-10 classification)	**Patients with T2DM n (%)**
Essential hypertension (I10)	2362 (49.4)
Disorders of lipoprotein metabolism and other lipidaemias (E78)	1612 (33.7)
Nontoxic thyroid nodule (E04)	1088 (22.8)
Fatty (change of) liver (K76)	984 (20.6)
Cataract (H26)	512 (10.7)
Chronic ischemic heart disease (I25)	455 (9.5)
Atherosclerosis (I70)	411 (8.6)
Osteoporosis (M81)	348 (7.3)
Cerebral infarction (I63)	341 (7.1)
Benign prostatic hyperplasia (N40)	303 (12.2*)
Abnormal findings on diagnostic imaging of lung (R91)	287 (6.0)
Thoracic, thoracolumbar, and lumbosacral intervertebral disc disorders (M51)	260 (5.4)
Obesity (E66)	177 (3.7)
Cervical disc disorders (M50)	161 (3.4)
Chronic viral hepatitis (B18)	138 (2.9)
Sleep disorders (G47)	135 (2.8)
Gout (M10)	132 (2.8)
Disorders of purine and pyrimidine metabolism (E79)	127 (2.7)
Atrial fibrillation and flutter (I48)	118 (2.5)
Gastro-oesophageal reflux disease (K21)	111 (2.3)

*In 2482 males.

Table 2. Characteristics of the study participants.

	Total (4777)	Comorbidity No (299) n (%)	Comorbidity Yes (4478) n (%)	Unadjusted OR (95% CI)	P value
Age (years)					<0.001
18-39	308	63 (20.5)	245 (79.5)	1	
40-59	1360	120 (8.8)	1240 (91.2)	2.66 (1.90,3.71)	
60-69	1289	75 (5.8)	1214 (94.2)	4.16 (2.90,5.98)	
≥70	1820	41 (2.3)	1779 (97.7)	11.16 (7.37,16.90)	
Sex					0.008
Male	2482	133 (5.4)	2349 (94.6)	1	
Female	2295	166 (7.2)	2129 (92.8)	0.73 (0.57,0.92)	
Education					0.005
University/college	545	47 (8.6)	498 (91.4)	1	
Class 7-12	1927	136 (7.1)	1791 (92.9)	1.24 (0.88,1.76)	
Class 1-6	1574	80 (5.1)	1494 (94.9)	1.76 (1.21,2.56)	
No qualification	731	36 (4.9)	695 (95.1)	1.82 (1.16,2.86)	
Occupation					<0.001
Manual worker	1088	74 (6.8)	1014 (93.2)	1	
Non-manual worker	1884	152 (8.1)	1732 (91.9)	0.83 (0.62,1.10)	
Never worked/retired	1805	73 (4.0)	1732 (96.0)	1.73 (1.24,2.41)	
Marital status					0.008
Married	4207	278 (6.6)	3929 (93.4)	1	
Single/divorced/widowed	570	21 (3.7)	549 (96.3)	1.85 (1.18,2.91)	
Residence					<0.001
Urban	2815	145 (5.2)	2670 (94.8)	1	
Rural	1962	154 (7.8)	1808 (92.2)	0.64 (0.50,0.81)	
Health insurance					<0.001
Yes	4211	232 (5.5)	3979 (94.5)	1	
No	564	67 (11.9)	497 (88.1)	0.43 (0.33,0.58)	
Smoking (current status)					0.073
No	3714	245 (6.6)	3469 (93.4)	1	
Yes	1063	54 (5.1)	1009 (94.9)	1.32 (0.98,1.79)	
Alcohol consumption (current status)					0.713
No	4169	263 (6.3)	3906 (93.7)	1	
Yes	608	36 (5.9)	572 (94.1)	1.07 (0.75,1.53)	
Duration of T2DM (years)					<0.001
≤1	981	93 (9.5)	888 (90.5)	1	
>1-5	880	60 (6.8)	820 (93.2)	1.43 (1.02,2.01)	
>5-10	1247	74 (5.9)	1173 (94.1)	1.66 (1.21,2.28)	
>10	1669	72 (4.3)	1597 (95.7)	2.32 (1.69,3.19)	
Blood glucose level (HbA1c)					0.458
<7%	899	64 (7.1)	835 (92.9)	1	

≥7%	3748	226 (6.0)	3522 (94.0)	1.19 (0.90,1.59)	
Unknown	130	9 (6.9)	121 (93.1)	1.03 (0.50,2.12)	

Table 3. Multiple backward stepwise logistic regression analysis for determining factors independently associated with comorbidity.

	Adjusted OR (95% CI)	P value
Age (years)		<0.001
18-39	1	
40-59	2.80 (1.98,3.96)	
60-69	4.43 (3.04,6.44)	
≥70	10.97 (7.17,16.77)	
Sex		<0.001
Male	1	
Female	0.66 (0.51,0.84)	
Marital status		0.006
Married	1	
Single/divorced/widowed	1.95 (1.21,3.12)	
Residence		0.018
Urban	1	
Rural	0.75 (0.59,0.95)	
Health insurance		0.002
Yes	1	
No	0.62 (0.46,0.83)	

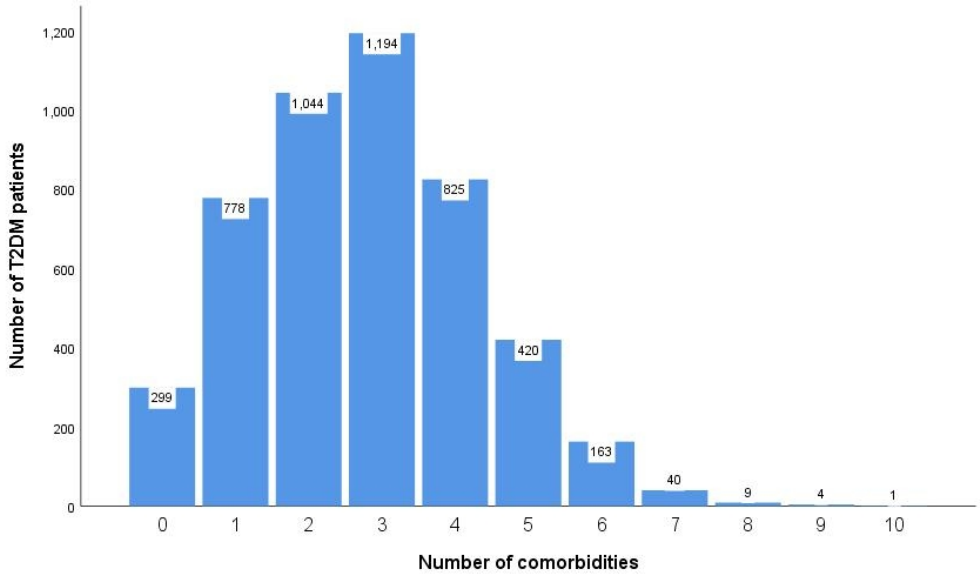

Figure 1. Number of comorbidities in our study.

300x176mm (72 x 72 DPI)

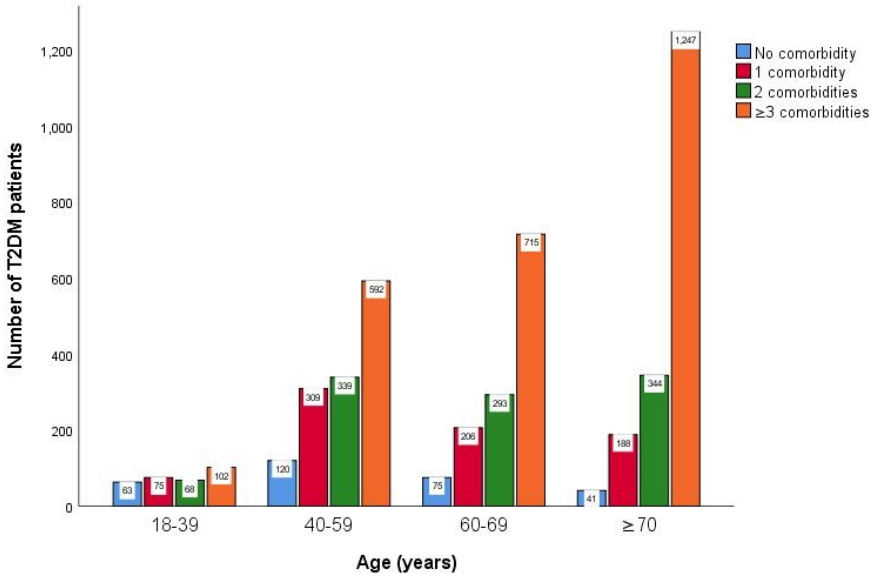

Figure 2. Number of comorbidities in our study in the different age groups.

300x176mm (72 x 72 DPI)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1,2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2,3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5,6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5,6
Bias	9	Describe any efforts to address potential sources of bias	5,6
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5,6,7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	n/a
		(*c*) Explain how missing data were addressed	7, Table2
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	n/a
		(*e*) Describe any sensitivity analyses	7
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5,7
		(b) Give reasons for non-participation at each stage	n/a
		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7, Table2
		(b) Indicate number of participants with missing data for each variable of interest	Table2
Outcome data	15*	Report numbers of outcome events or summary measures	7, Figure 1, Figure 2, Table1, Table2
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7, 8, Table2
		(*b*) Report category boundaries when continuous variables were categorized	7, 8, Table2, Table3
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	7, 8
Discussion			
Key results	18	Summarise key results with reference to study objectives	8, 9, 10, 11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10, 11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	8, 9, 10, 11
Generalisability	21	Discuss the generalisability (external validity) of the study results	11
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	11

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Prevalence of comorbidities and their associated factors in patients with type 2 diabetes at a tertiary care department in Ningbo, China: a cross-sectional study

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Title

Prevalence of comorbidities and their associated factors in patients with type 2 diabetes at a tertiary care department in Ningbo, China: a cross-sectional study

Xueyu Li*[1, 2], Kaushik Chattopadhyay*[3], Shengnan Xu[2], Yanshu Chen[2], Miao Xu[2], Li Li[2], Jialin Li[2]

[1]Ningbo University Medical School, Ningbo, PR China

[2]Department of Endocrinology and Metabolism, Ningbo First Hospital, Ningbo, PR China

[3]Division of Epidemiology and Public Health, School of Medicine, University of Nottingham, Nottingham, UK

*These authors contributed equally to this work.

Corresponding author: Dr Jialin Li, e-mail; lijialin@sina.com

Abstract

Objectives To determine the prevalence of comorbidities in patients with type 2 diabetes (T2DM) and identify the factors independently associated with comorbidities in a tertiary care department in Ningbo, China.

Design A computerised medical records database was used to conduct a cross-sectional study.

Setting The study was conducted in a tertiary care department in Ningbo, China.

Participants The study was conducted on adult patients with T2DM, and it included eight years of data, from 1 January 2012 to 31 December 2019.

The primary outcome measure Comorbidity was defined as the co-existence of at least one other chronic condition, i.e., either a physical non-communicable disease (duration ≥3 months), a mental health condition (duration ≥3 months), or an infectious disease (duration ≥3 months).

Results In total, 4777 patients with T2DM satisfied the eligibility criteria. Over eight years, the prevalence of comorbidities was 93.7%. The odds of comorbidities increased with the age of patients (18–39 years: 1; 40–59 years: odds ratio 2.80, 95% confidence interval 1.98–3.96; 60–69 years: 4.43, 3.04–6.44; and ≥70 years: 10.97, 7.17–16.77). The odds were lower in female patients (0.66, 0.51–0.84), patients residing in rural areas (0.75, 0.59–0.95), and patients without health insurance (0.62, 0.46–0.83). The odds were higher in single/divorced/widowed patients compared to those in married patients (1.95, 1.21–3.12).

Conclusions A large percentage of patients with T2DM in the tertiary care department in Ningbo, China, had comorbidities, and the factors associated with comorbidities were identified. The findings could be used in developing, evaluating, and

implementing interventions aimed at improving outcomes in patients with T2DM with comorbidities.

Keywords

comorbidity, type 2 diabetes, China

Strengths and limitations of the study

- Ours was the first study to investigate comorbidities in patients with type 2 diabetes in Ningbo and the broader Zhejiang Province of China.
- We included all the chronic conditions in our study; they were coded using the International Classification of Diseases, 10th edition (ICD-10) in our database.
- Our study had extremely low missing data and the multiple logistic regression analysis included a sample with missing data for the adjusted variable.
- As it was a cross-sectional study, the causal relationship between the variables and the comorbidities could not be determined.
- The high prevalence of comorbidities in our study could be due to the study setting (i.e., hospital).

INTRODUCTION

Ningbo is an economically developed Chinese city in Zhejiang Province. The population of the city is approximately 8.2 million.[1] Non-communicable diseases are prevalent in the city, and one of the most prevalent non-communicable diseases is type 2 diabetes (T2DM), a complex metabolic disorder.[2] China has the largest T2DM epidemic in the world, and in Ningbo, its prevalence in adults ⩾ 40 years of age is 21%.[3] In Ningbo, the diabetes-related mortality is 14.5 per 100,000 population.[4]

There is no international consensus regarding the best way to define comorbidity. It is usually defined as the co-existence of other conditions with an index condition (i.e., the main condition under study) where these other conditions are not consequences of the index condition.[5-7] Comorbidities accelerate the progression of individual conditions, encourage the development of other physical and mental conditions, and even lead to premature mortality.[8-10] Moreover, they negatively affect overall health, wellbeing, and functioning.[11, 12] Additionally, they lead to high treatment burden, high healthcare utilisation and expenditure, and loss of economic output.[13, 14] In real life, T2DM is rarely presented in isolation and is always accompanied by comorbidity.[15, 16]

To date, no study has been undertaken to investigate comorbidities in patients with T2DM in Ningbo. The study objectives were to determine the prevalence of comorbidities in patients with T2DM and identify the factors independently associated with comorbidities. This knowledge could be used in developing, evaluating, and implementing interventions aimed at improving outcomes in patients with T2DM with comorbidities.

METHODS

Study location, study design, data source, and study period

We conducted the study in a tertiary care department, the Department of Endocrinology and Metabolism, Ningbo First Hospital, in Ningbo, China. This tertiary care hospital delivers speciality healthcare services, provides medical education, and conducts research.[17,18] Locals and people from the surrounding areas visit this hospital as no referral is required from the general practitioner.[17] An existing computerised medical records database was used for conducting this cross-sectional study. This database contained information on all inpatients. Since it was a real-time database, new patients were added continuously. Data were entered by the medico-nursing team and an independent group of the hospital staff was responsible for assessing the quality of the data and overall database management. All the conditions were coded using the International Classification of Diseases, 10th edition (ICD-10). This retrospective study included eight years of data, from 1 January 2012 to 31 December 2019, and the information was available on 6755 patients.

Study population and study inclusion and exclusion criteria

Adult patients (≥ 18 years) with T2DM were included. If a patient was admitted more than once during the study period, data pertinent to the last admission were extracted to obtain the most recent information on health conditions. Individuals with gestational diabetes, type 1 diabetes, secondary diabetes, and unknown types of diabetes were excluded.

Study variables

We extracted and categorised the following information from the database:

- age (18–39 years, 40–59 years, 60–69 years or ≥70 years),
- sex (male or female),
- education (university/college, class 7–12, class 1–6, or no qualification),
- occupation (manual worker [i.e., more physical work than mental work], non-manual worker [i.e., more mental work than physical work], or never worked/retired),

- marital status (married or single/divorced/widowed),
- residence (urban or rural using the “hukou” system i.e., the Chinese household registration system),
- health insurance,
- smoking (current status),
- alcohol consumption (current status),
- duration of T2DM (≤ 1 year, > 1–5 years, > 5–10 years, or > 10 years), and
- blood glucose level (glycated haemoglobin [HbA1c < 7% (good) or ≥ 7% (poor)], estimated using the high-performance liquid chromatographic method and D-10 Haemoglobin Analyser [Bio-Rad, USA]). In China, the recommended HbA1c treatment target did not change over the study period (< 7% for most patients with T2DM).[19-21]

In addition, information on comorbidities was extracted. The index condition was T2DM. Comorbidity was defined as the co-existence of at least one other chronic condition, i.e., either a physical non-communicable disease (duration ≥ 3 months), a mental health condition (duration ≥ 3 months), or an infectious disease (duration ≥ 3 months).[5-7] T2DM-specific complications (i.e., microvascular complications, such as diabetic retinopathy, nephropathy, and neuropathy/foot) were excluded as these were consequences of the index condition; hence, they were not considered as comorbidities.[6]

Ethics

The Research Ethics Committee of the Ningbo First Hospital, China, approved this study (2020-R106). The researchers had no access to information that could identify individual patients during the data analyses. No informed consent was required as per research ethics rules.

Patient and public involvement

Patients and the public were not involved in the study.

Statistical analyses

We calculated numbers and percentages for categorical variables and means and standard deviations (SDs) for normally distributed continuous variables. We used a simple logistic regression method to investigate the association between the different variables and comorbidities. We developed a multiple logistic regression model to identify any independent associations. For this, we used backward stepwise regression analysis and included all the variables. Additionally, we performed a sensitivity analysis — in the multiple logistic regression model, we included only those variables that had a p-value ≤ 0.20 in simple logistic regressions. We calculated odds ratios (ORs) and 95% confidence intervals (CIs). We used IBM SPSS Statistics version 26.0 for Windows for statistical analyses.

RESULTS

A total of 4777 patients with T2DM satisfied the eligibility criteria. The mean (±SD) age of patients was 64.2 (±14.2) years, and approximately 52% (n=2482) of them were men. The mean (±SD) HbA1c level was 9.2% (±2.4%). Over eight years, the prevalence of comorbidities was 93.7%. The year-wise prevalences from 2012 to 2019 were 96.9%, 95.0%, 92.9%, 95.5%, 93.2%, 91.5%, 94.0%, and 93.6%, respectively.

Figure 1 shows the number of comorbidities in our study. The mean (±SD) number of comorbidities was 3 (±1). Figure 2 shows the percentage of comorbidities in our study in the different age groups. In the ⩾ 70 years age group, 68.5% (1247) had ⩾ 3 comorbidities, whereas the prevalences were only 33.1% (102), 43.5% (592), and 55.5% (715) in the 18–39, 40–59, and 60–69 years age groups, respectively. Table 1 reports the most common comorbidities in our study. Essential hypertension (49.4%), disorders of lipoprotein metabolism and other lipidaemias (33.7%), nontoxic thyroid nodule (22.8%), fatty change of liver (20.6%), and cataract (10.7%) were the five most

prevalent comorbidities.

Table 2 reports the characteristics of the study participants. We found that the comorbidities were associated with age, sex, education, occupation, marital status, residence, health insurance, and the duration of T2DM. Table 3 reports the multiple backward stepwise logistic regression analysis for determining factors independently associated with the comorbidities. The odds of comorbidities increased with the age of patients (18–39 years: 1; 40–59 years: OR 2.80, 95% CI 1.98–3.96; 60–69 years: 4.43, 3.04–6.44; and ≥70 years: 10.97, 7.17–16.77). The odds were lower in female patients (0.66, 0.51–0.84), patients residing in rural areas (0.75, 0.59–0.95), and patients without health insurance (0.62, 0.46–0.83). The odds were higher in single/divorced/widowed patients compared to married patients (1.95, 1.21–3.12). We obtained similar results in the sensitivity analysis.

DISCUSSION

In our tertiary care department in Ningbo, China, approximately 94% of the patients with T2DM had comorbidities and this influenced the overall management. In a previous study, we found that approximately 72% of the patients with T2DM were prescribed polypharmacy.[22] There are no similar studies on comorbidities conducted in patients with T2DM in China published in the English language. However, we found two similar studies published in Mandarin: one on patients with diabetes at a community health centre and another on outpatients with T2DM at a tertiary care hospital.[23, 24] The corresponding prevalence figures were around 95% and 73%, respectively. The different prevalence figures could be explained by the differences in population characteristics, the study setting, and the definition of comorbidity applied. Several studies have been conducted on this subject in high-income countries such as the United States and European countries.[25-29] All these studies, and also our study, have highlighted the fact that comorbidities are highly prevalent in patients with T2DM. A systematic review and meta-analysis of the prevalence of comorbidities in patients

with T2DM in different geographical locations and the factors associated with it will be helpful.

Comorbidities are not synonymous with complications.[6] In a previous study on the vascular complications of T2DM, we included microvascular complications (i.e., diabetic retinopathy, nephropathy, and neuropathy/foot) and macrovascular complications (i.e., coronary heart disease, stroke, and peripheral arterial disease) and found that more than half of the patients with T2DM had vascular complications.[30] In the present study, we explored comorbidities in patients with T2DM using a recommended definition. Comorbidity was defined as the co-existence of at least one other chronic condition, either a physical (non-communicable/infectious disease) or mental health condition.[5-7] Unlike the previous study, in the present study, microvascular complications were excluded, as these were consequences of T2DM and should not be considered as comorbidities.[6] Although human immunodeficiency virus (HIV) infection, tuberculosis (TB) and mental health conditions are common comorbidities in patients with T2DM,[31-34] these were not the most common comorbidities in this study. The prevalences of these infectious diseases are low in Ningbo,[35-38] and there are chances that mental health conditions were underreported. It should also be noted that infectious diseases and mental health conditions as index conditions are treated in other specialised hospitals in Ningbo.

We found that the odds of comorbidities increased with age in patients with T2DM. Age is one of the most well-studied and consistent determinants of comorbidities.[25, 28,39] Age-related organ degeneration is a natural process and can lead to the development of many health conditions.[40] However, it should be noted that comorbidities do not correspond with age and they are not limited to the older population alone.[41] In our study, the prevalences of comorbidities were around 80% and 91% in the 18–39 and 40–59 years age groups, respectively. We found that the odds of comorbidities were lower in female patients with T2DM compared with those in their male counterparts. This finding is consistent with other studies.[25, 28] This could be due to differences at

the biological level. Another potential reason could be the reporting differences in sex-specific health conditions. For example, female patients with T2DM often present with atypical symptoms of cardiovascular diseases.[42] Additionally, the standard non-invasive diagnostic tests perform better in men than in women.[43] All these hinder the diagnosis of cardiovascular diseases in women. Another example is benign prostatic hyperplasia, one of the most common comorbidities in our study. This comorbidity was diagnosed because of the compulsory ultrasound scan of the urinary system of patients with T2DM at our hospital for possible kidney diseases. In comparison, the gynaecological examination is not a routine examination in women with T2DM.

We found that the odds of comorbidities were lower in patients with T2DM residing in rural areas compared to those in urban areas. This could be due to economic growth, urbanisation, and its negative consequences such as an unhealthy lifestyle.[44-46] The link between an unhealthy lifestyle and chronic conditions (particularly non-communicable diseases) is well established.[47] A similar association has also emerged with comorbidities.[23,48] Another reason could be that rural patients in China have limited access to healthcare and thus, they may undergo fewer diagnostic tests and obtain fewer confirmations of health conditions.[49] We found that the odds of comorbidities were lower in patients with T2DM without health insurance compared to those with health insurance. This could be due to the fact that over 90% of the Chinese population have some sort of health insurance,[50] and these patients may undergo more diagnostic tests (within the scope of their health insurance policy) and obtain confirmation of a range of health conditions.[51] We found that the odds of comorbidities were higher in single/divorced/widowed patients with T2DM compared with those in married patients. In general, the spouses of married patients provide both physical and mental support to them, and this could help them manage their existing health conditions and prevent new ones from emerging.[52,53]

This study has several strengths and weaknesses. Comorbidity is a less-explored area in China, and to the best of our knowledge, this was the first study to explore

comorbidities in patients with T2DM in Ningbo and the broader Zhejiang Province. The quality of our routinely collected data was good. Unlike other studies where comorbidities in T2DM were self-reported by the patients with T2DM using a predetermined list of selected comorbidities,[23, 24] we used a holistic approach. All the conditions were coded using the International Classification of Diseases, 10th edition (ICD-10) in our database, and we included all the chronic conditions in our study. This also minimised the possibility of recall bias in our study. Our study had extremely low missing data; only HbA1c data were missing in 130 patients out of 4777 (i.e., 2.7%). Multiple logistic regression analysis included a sample with missing data for the adjusted variable. Since it was a cross-sectional study, the causal relationship between variables and comorbidities could not be determined. We propose to conduct a longitudinal study to explore the effects of various factors on comorbidities, including factors considered in this study and other factors such as physical activity and diet that were not present in our database and could not be adjusted for in the models. In our study, the high prevalence of comorbidities could be due to the study setting (i.e., hospital). The findings of our hospital-based study could be valid in similar settings. We suggest conducting a population-based study that might provide a distinct picture of the issue in Ningbo.

In conclusion, we found that a large percentage of patients with T2DM in the tertiary care department in Ningbo, China, had comorbidities, and we also identified the factors associated with comorbidities. The findings could be used in developing, evaluating, and implementing interventions aimed at improving outcomes in patients with T2DM with comorbidities.

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CONTRIBUTORS JL and KC designed the study. XL and KC analysed the data and wrote the first draft of the manuscript. SX and YC contributed to patient registration

and data entry. XL contributed to data cleaning. XL, KC, SX, YC, MX, LL and JL revised it critically for important intellectual content and approved the final version.

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COMPETING INTERESTS None declared.

ETHICS APPROVAL The Research Ethics Committee of Ningbo First Hospital, China approved the study (2020-R106).

DATA SHARING STATEMENT The dataset will be available upon request unless there are legal or ethical reasons for not doing so.

REFERENCES

1. Ningbo Municipal Statistics Bureau. Statistical Bulletin on National Economic and Social Development in Ningbo, China, 2018.

2. Health and Family Planning Commission of Ningbo Municipality. Prevention and treatment of chronic diseases in Ningbo. http://www.cnnb.com.cn/nbzfxwfbh/system/2014/05/22/008068694.shtml (accessed 25 Apr 2020).

3. Yao DZ, Sun XH, Li JH. Prevalence and risk factors of diabetes in people over 40 years of age in Ningbo city area. *Modern Practical Medicine* 2016;28:1343-5.

4. Li H, Cui J, Gong J, *et al*. Diabetes morbidity and mortality of residents in Ningbo, 2010-2014. *Chinese Rural Health Service Administration* 2016;36:1304-7.

5. World Health Organization. *Multimorbidity*. Geneva: Switzerland, 2016.

6. Ording AG, Sørensen HT. Concepts of comorbidities, multiple morbidities, complications, and their clinical epidemiologic analogs. *Clin Epidemiol* 2013;5:199-203.

7. Valderas JM, Starfield B, Sibbald B, *et al*. Defining comorbidity: implications for understanding health and health services. *Ann Fam Med* 2009;7:357-63.

8. Einarson TR, Acs A, Ludwig C, *et al*. Prevalence of cardiovascular disease in type 2 diabetes: a systematic literature review of scientific evidence from across the world in 2007-2017. *Cardiovasc Diabetol* 2018;17:83.

9. Nouwen A, Winkley K, Twisk J, *et al*. Type 2 diabetes mellitus as a risk factor for the onset of depression: a systematic review and meta-analysis. *Diabetologia* 2010;53:2480-6.

10. Yokomichi H, Nagai A, Hirata M, *et al*. Survival of macrovascular disease, chronic kidney disease, chronic respiratory disease, cancer and smoking in patients with type 2 diabetes: BioBank Japan cohort. *J Epidemiol* 2017;27:S98-S106.

11. Adriaanse MC, Drewes HW, van der Heide I, *et al*. The impact of comorbid chronic conditions on quality of life in type 2 diabetes patients. *Qual Life Res* 2016;25:175-82.

12. Wermeling PR, Gorter KJ, van Stel HF, *et al*. Both cardiovascular and non-cardiovascular comorbidity are related to health status in well-controlled type 2 diabetes patients: a cross-sectional analysis. *Cardiovasc Diabetol* 2012;11:121.

13. Gruneir A, Markle-Reid M, Fisher K, *et al*. Comorbidity burden and health services use in community-living older adults with diabetes mellitus: a retrospective cohort study. *Can J Diabetes* 2016;40:35-42.

14. Terauchi Y, Ozaki A, Zhao XH, *et al*. Humanistic and economic burden of cardiovascular disease related comorbidities and hypoglycaemia among patients with type 2 diabetes in Japan. *Diabetes Res Clin Pract* 2019;149:115-25.

15. Australian Bureau of Statistics. *National Health Survey: First Result, 2014-15.* Canberra: Australian, 2015.

16. Druss BG, Marcus SC Olfson M, *et al*. Comparing the national economic burden of five chronic conditions. *Health Aff (Millwood)* 2001;20:233-41.

17. Ningbo First Hospital. Hospital Introduction. http://www.nbdyyy.com/col/col100/index.html (accessed 25 Apr 2020).

18. Ministry of Health of the People's Republic of China. *The measures for the administration of the hospital grade*. Beijing: Ministry of Health of the People's Republic of China, 1989.

19. Chinese Diabetes Society. China guideline for type 2 diabetes (2010 ed). *Chin J Diabetes* 2012;20:S1-S36.

20. Chinese Diabetes Society. China guideline for type 2 diabetes (2013 ed). *Chin J Endocrinol Metab* 2014;30:893-942.

21. Jia W, Weng J, Zhu D, *et al*. Standards of medical care for type 2 diabetes in China 2019. *Diabetes Metab Res Rev* 2019;35:e3158.

22. Li J, Chattopadhyay K, Xu M, *et al*. Prevalence and predictors of polypharmacy prescription among type 2 diabetes patients at a tertiary care department in Ningbo, China: a retrospective database study. *PLoS One* 2019;14:e0220047.

23. Xing Y, Wang P, Yang X. A survey of comorbidity and health behaviors of diabetic patients in an area of Beijing. *Journal of Chinese Physician* 2020;22:379-84.

24. Zhao W, Zhao D, Wang X, *et al*. Current status and influential factors of co-morbidity for patients with type 2 diabetes mellitus in Tongzhou district of Beijing. *Chin J Health Manage* 2019;13:541-5.

25. Alonso-Morán E, Orueta JF, Esteban JI, *et al*. Multimorbidity in people with type 2 diabetes in the Basque country (Spain): prevalence, comorbidity clusters and comparison with other chronic patients. *Eur J Intern Med* 2015;26:197-202.

26. Lin PJ, Kent DM, Winn A, *et al*. Multiple chronic conditions in type 2 diabetes mellitus: prevalence and consequences. *Am J Manag Care* 2015;21:e23-34.

27. Teljeur C, Smith SM, Paul G, *et al*. Multimorbidity in a cohort of patients with type 2 diabetes. *Eur J Gen Pract* 2013;19:17-22.

28. Iglay K, Hannachi H, Howie PJ, *et al*. Prevalence and co-prevalence of comorbidities among patients with type 2 diabetes mellitus. *Curr Med Res Opin* 2016;32:1243-52.

29. Hermans MP, Dath N. Prevalence and co-prevalence of comorbidities in Belgian patients with type 2 diabetes mellitus: a transversal, descriptive study. *Acta Clin Belg* 2018;73:68-74.

30. Li J, Chattopadhyay K, Xu M, *et al*. Prevalence and associated factors of vascular complications among inpatients with type 2 diabetes: a retrospective database study at a tertiary care department, Ningbo, China. *PloS One* 2020;15:e0235161.

31. Workneh MH, Bjune GA, Yimer SA. Prevalence and associated factors of tuberculosis and diabetes mellitus comorbidity: a systematic review. *PloS One* 2017;12:e0175925.

32. Berkowitz N, Okorie A, Goliath R, *et al*. The prevalence and determinants of active

tuberculosis among diabetes patients in Cape Town, South Africa, a high HIV/TB burden setting. *Diabetes Res Clin Pract* 2018;138:16-25.

33. Hadigan C, Kattakuzhy S. Diabetes mellitus type 2 and abnormal glucose metabolism in the setting of human immunodeficiency virus. *Endocrinol Metab Clin North Am* 2014;43:685-96.

34. Garrett C, Doherty A. Diabetes and mental health. *Clin Med (Lond)* 2014;14:669-72.

35. Yang T, Chen T, Che Y, *et al*. Factors associated with catastrophic total costs due to tuberculosis under a designated hospital service model: a cross-sectional study in China. *BMC Public Health* 2020;20:1009.

36. Liu K, Li T, Vongpradith A, *et al*. Identification and prediction of tuberculosis in eastern China: analyses from 10-year population-based notification data in Zhejiang province, China. *Sci Rep* 2020;10:7425.

37. Zhang JH, Li HL, Shi HB, *et al*. Survival analysis of HIV/AIDS patients with access to highly antiretroviral therapy in Ningbo during 2004-2015. *Zhonghua Liu Xing Bing Xue Za Zhi* 2016;37:1262-7.

38. Ministry of Health of the People's Republic of China, UNAIDS, WHO. Estimation for HIV/AIDS epidemic trend in 2011, China. *Chin J AIDS STD* 2012;18:1-5.

39. Mata-Cases M, Franch-Nadal J, Real J, *et al*. Prevalence and coprevalence of chronic comorbid conditions in patients with type 2 diabetes in Catalonia: a population-based cross-sectional study. *BMJ Open* 2019;9:e031281.

40. King M, Lipsky MS. Clinical implications of aging. *Dis Mon* 2015;61:467-74.

41. van Oostrom SH, Gijsen R, Stirbu I, *et al*. Time trends in prevalence of chronic diseases and multimorbidity not only due to aging: data from general practices and health surveys. *PLoS One* 2016;11:e0160264.

42. Wada H, Miyauchi K, Daida H. Gender Differences in the clinical features and outcomes of patients with coronary artery disease. *Expert Rev Cardiovasc Ther* 2019;17:127-33.

43. Shah AS, Griffiths M, Lee KK, *et al*. High sensitivity cardiac troponin and the under-diagnosis of myocardial infarction in women: prospective cohort study. *BMJ* 2015;350:g7873.

44. Zhu W, Chi A, Sun Y. Physical activity among older Chinese adults living in urban

and rural areas: a review. *J Sport Health Sci* 2016;5:281-6.

45. Muntner P, Gu D, Wildman RP, *et al*. Prevalence of physical activity among Chinese adults: results from the international collaborative study of cardiovascular disease in Asia. *Am J Public Health* 2005;95:1631-6.

46. Miao J, Wu X. Urbanization, socioeconomic status and health disparity in China. *Health Place* 2016;42:87-95.

47. World Health Organization. *Global action plan for the prevention and control of NCD 2013-2020*. Geneva: Switzerland, 2013.

48. Wang X. Chen J, Liu X, *et al*. Identifying patterns of lifestyle behaviors among people with type 2 diabetes in Tianjin, China: a latent class analysis. *Diabetes Ther* 2017;8:1379-92.

49. Liu Z, Albanese E, Li S, *et al*. Chronic disease prevalence and care among the elderly in urban and rural Beijing, China - a 10/66 dementia research group cross-sectional survey. *BMC Public Health* 2009;9:394.

50. Zhao C, Wang C, Shen C, *et al*. China's achievements and challenges in improving health insurance coverage. *Drug Discov Ther* 2018;12:1-6.

51. Yang C, Huang Z, Sun K, *et al*. Comparing the economic burden of type 2 diabetes mellitus patients with and without medical insurance: a cross-sectional study in China. *Med Sci Monit* 2018;24:3039-102.

52. Stroebe M, Schut H, Stroebe W. Health outcomes of bereavement. *Lancet* 2007; 370:1960-73.

53. Parajuli J, Saleh F, Thapa N, Ali L. Factors associated with nonadherence to diet and physical activity among Nepalese type 2 diabetes patients: a cross sectional study. *BMC Res Notes* 2014;7:758.

Figure 1. Number of comorbidities in our study.

Figure 2. Percentage of comorbidities in our study in the different age groups.

Table 1. Most common comorbidities in our study.

Most common comorbidities (based on ICD-10 classification)	Patients with T2DM n (%)
Essential hypertension (I10)	2362 (49.4)
Disorders of lipoprotein metabolism and other lipidaemias (E78)	1612 (33.7)
Nontoxic thyroid nodule (E04)	1088 (22.8)
Fatty (change of) liver (K76)	984 (20.6)
Cataract (H26)	512 (10.7)
Chronic ischemic heart disease (I25)	455 (9.5)
Atherosclerosis (I70)	411 (8.6)
Osteoporosis (M81)	348 (7.3)
Cerebral infarction (I63)	341 (7.1)
Benign prostatic hyperplasia (N40)	303 (12.2*)
Abnormal findings on diagnostic imaging of lung (R91)	287 (6.0)
Thoracic, thoracolumbar, and lumbosacral intervertebral disc disorders (M51)	260 (5.4)
Obesity (E66)	177 (3.7)
Cervical disc disorders (M50)	161 (3.4)
Chronic viral hepatitis (B18)	138 (2.9)
Sleep disorders (G47)	135 (2.8)
Gout (M10)	132 (2.8)
Disorders of purine and pyrimidine metabolism (E79)	127 (2.7)
Atrial fibrillation and flutter (I48)	118 (2.5)
Gastro-oesophageal reflux disease (K21)	111 (2.3)

*In 2482 males.

Table 2. Characteristics of the study participants.

	Total (4777)	Comorbidity No (299)	Comorbidity Yes (4478)	Unadjusted OR (95% CI)	P value

		n (%)	n (%)		
Age (years)					<0.001
18-39	308	63 (20.5)	245 (79.5)	1	
40-59	1360	120 (8.8)	1240 (91.2)	2.66 (1.90,3.71)	
60-69	1289	75 (5.8)	1214 (94.2)	4.16 (2.90,5.98)	
≥70	1820	41 (2.3)	1779 (97.7)	11.16 (7.37,16.90)	
Sex					0.008
Male	2482	133 (5.4)	2349 (94.6)	1	
Female	2295	166 (7.2)	2129 (92.8)	0.73 (0.57,0.92)	
Education					0.005
University/college	545	47 (8.6)	498 (91.4)	1	
Class 7-12	1927	136 (7.1)	1791 (92.9)	1.24 (0.88,1.76)	
Class 1-6	1574	80 (5.1)	1494 (94.9)	1.76 (1.21,2.56)	
No qualification	731	36 (4.9)	695 (95.1)	1.82 (1.16,2.86)	
Occupation					<0.001
Manual worker	1088	74 (6.8)	1014 (93.2)	1	
Non-manual worker	1884	152 (8.1)	1732 (91.9)	0.83 (0.62,1.10)	
Never worked/retired	1805	73 (4.0)	1732 (96.0)	1.73 (1.24,2.41)	
Marital status					0.008
Married	4207	278 (6.6)	3929 (93.4)	1	
Single/divorced/widowed	570	21 (3.7)	549 (96.3)	1.85 (1.18,2.91)	
Residence					<0.001
Urban	2815	145 (5.2)	2670 (94.8)	1	
Rural	1962	154 (7.8)	1808 (92.2)	0.64 (0.50,0.81)	
Health insurance					<0.001
Yes	4211	232 (5.5)	3979 (94.5)	1	
No	564	67 (11.9)	497 (88.1)	0.43 (0.33,0.58)	
Smoking (current status)					0.073
No	3714	245 (6.6)	3469 (93.4)	1	
Yes	1063	54 (5.1)	1009 (94.9)	1.32 (0.98,1.79)	
Alcohol consumption (current status)					0.713
No	4169	263 (6.3)	3906 (93.7)	1	
Yes	608	36 (5.9)	572 (94.1)	1.07 (0.75,1.53)	
Duration of T2DM (years)					<0.001
≤1	981	93 (9.5)	888 (90.5)	1	
>1-5	880	60 (6.8)	820 (93.2)	1.43 (1.02,2.01)	
>5-10	1247	74 (5.9)	1173 (94.1)	1.66 (1.21,2.28)	
>10	1669	72 (4.3)	1597 (95.7)	2.32 (1.69,3.19)	
Blood glucose level (HbA1c)					0.458
<7%	899	64 (7.1)	835 (92.9)	1	
≥7%	3748	226 (6.0)	3522 (94.0)	1.19 (0.90,1.59)	
Unknown	130	9 (6.9)	121 (93.1)	1.03 (0.50,2.12)	

Table 3. Multiple backward stepwise logistic regression analysis for determining factors independently associated with comorbidity.

	Adjusted OR (95% CI)	P value
Age (years)		<0.001
18-39	1	
40-59	2.80 (1.98,3.96)	
60-69	4.43 (3.04,6.44)	
≥70	10.97 (7.17,16.77)	
Sex		<0.001
Male	1	
Female	0.66 (0.51,0.84)	
Marital status		0.006
Married	1	
Single/divorced/widowed	1.95 (1.21,3.12)	
Residence		0.018
Urban	1	
Rural	0.75 (0.59,0.95)	
Health insurance		0.002
Yes	1	
No	0.62 (0.46,0.83)	

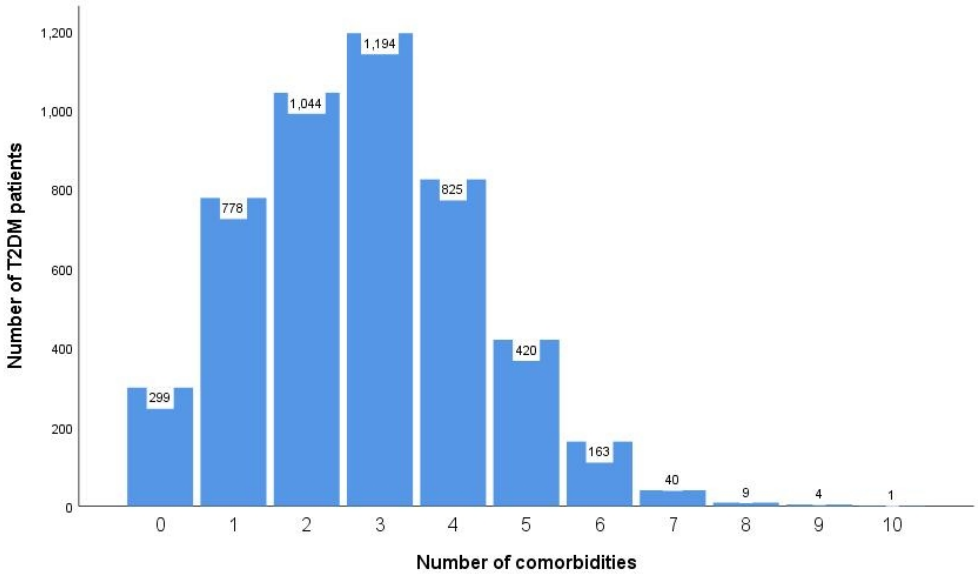

Figure 1. Number of comorbidities in our study.

300x176mm (72 x 72 DPI)

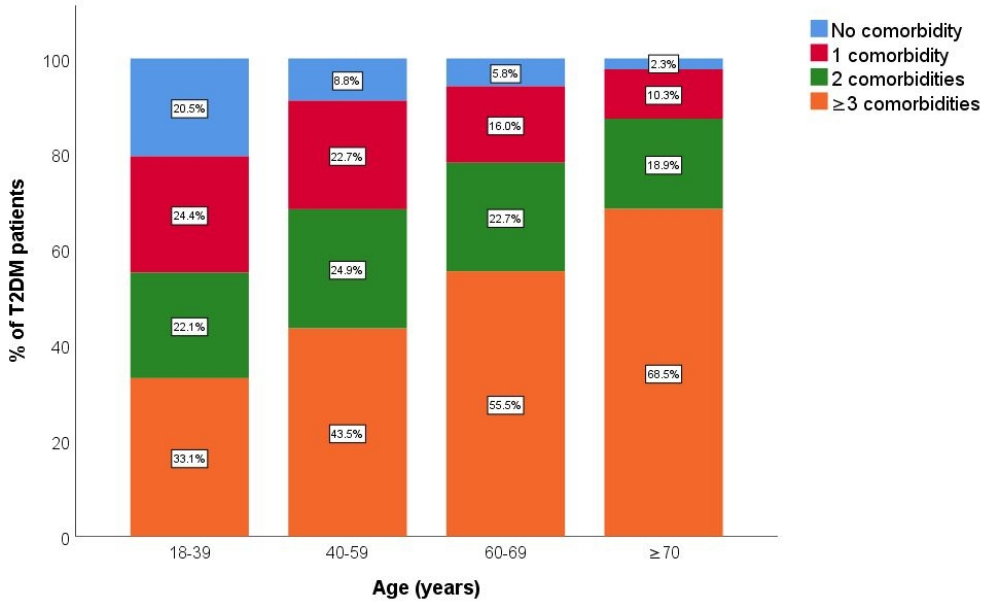

Figure 2. Percentage of comorbidities in our study in the different age groups

256x159mm (96 x 96 DPI)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1,2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2,3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5,6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5,6
Bias	9	Describe any efforts to address potential sources of bias	5,6
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5,6,7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	n/a
		(*c*) Explain how missing data were addressed	7, Table2
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	n/a
		(*e*) Describe any sensitivity analyses	7
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5,7
		(b) Give reasons for non-participation at each stage	n/a
		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7, Table2
		(b) Indicate number of participants with missing data for each variable of interest	Table2
Outcome data	15*	Report numbers of outcome events or summary measures	7, Figure 1, Figure 2, Table1, Table2
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7, 8, Table2
		(*b*) Report category boundaries when continuous variables were categorized	7, 8, Table2, Table3
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	7, 8
Discussion			
Key results	18	Summarise key results with reference to study objectives	8, 9, 10, 11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10, 11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	8, 9, 10, 11
Generalisability	21	Discuss the generalisability (external validity) of the study results	11
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	11

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.