Chapter 2 Association between triglycerides and insulin resistance as a predictor of cardiometabolic diseases in university students

Capítulo 2 Asociación de triglicéridos con resistencia a la insulina como predictor de enfermedades cardiometabólicas en universitarios

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Abstract

Cardiometabolic diseases represents the main cause of death in the world and several risk factors influence in different way. On the other hand, those risk factors appear at younger ages each time. One common factor is the insulin resistance and dyslipidemia. Some studies have suggested that higher levels of triglycerides are an independent risk factor for insulin resistance and in the future the possible development of diabetes and cardiovascular diseases. We performed a cross sectional study. Obtaining data of 189 university students from the faculty of pharmacy. Which 30% presented insulin resistance and 17% hypertriglyceridemia. We obtained an OR of 3.890 (IC 1.711-8.45; p<0.0004). Identify at early stage the possible risk factors for cardiometabolic disease comes important for the prevention of the same disease.

Triglycerides, Cardiovascular, Resistance

Resumen

Las enfermedades cardiometabólicas representan la principal causa de muerte en el mundo y los diversos factores de riesgo influyen en diferente magnitud. Por otro lado, estos factores se presentan cada vez a más temprana edad. Un común denominador de estos padecimientos es la resistencia a la insulina y las dislipidemias. Diversos estudios han sugerido que niveles elevados de triglicéridos son un factor de riesgo independiente de resistencia a la insulina y en un futuro el posible desarrollo de diabetes y enfermedades cardiovasculares. Se realizó un estudio de tipo transversal analítico. Se obtuvieron datos de 189 estudiantes universitarios de la Facultad de Farmacia. De estos el 30 % presentó resistencia a la insulina y el 17% hipertrigliceridemia. Se obtuvo un OR de 3.890 (IC 1.771-8.545; p <0.0004). Identificar de manera temprana posibles factores de riesgo modificables de enfermedades cardiometabólicas resulta de vital importancia para la prevención temprana de las mismas.

Triglicéridos, Cardiovascular, Resistencia

2.1 Introduction

The prevalence of cardio-metabolic diseases and their associated consequences is currently increasing (Weschenfelder *et al*., 2020). Of these, cardiovascular diseases (CVD) constitute a major public health problem. In the last decade, the number of deaths from CVD has increased worldwide by 12.5% over the previous decade (Joseph P. *et al.,* 2020). Diseases of the cardiovascular system are now the leading cause of death in the world's adult population (World Health Organization, 2017).

In some regions of the world, including Latin America, life expectancy at birth continues to increase; however, the quality of life in many cases does not increase at the same rate, due to the large number of health complications that go from chronic diseases, caused by the consumption of diets high in saturated fats to smoking and sedentary lifestyles; these facts become more common and result in high mortality from CVD (Pan American Health Organization, 2017).

CVD is multifactorial in origin and one risk factor must be considered to interfere in the context of others. Cardiovascular risk factors (CVRFs) are a set of biological characteristics or behaviors that, in those individuals who exhibit them, increase the likelihood of developing or dying from CVD (Baeradeh *et al*., 2022). The WHO considers smoking, a sedentary lifestyle, a diet low in fiber and high in cholesterol and saturated fat, DM2, dyslipidemia and high blood pressure as the main modifiable cardiometabolic risk factors (Wu Y. *et al*., 2014). Of these factors, dyslipidemia, and insulin resistance as a precursor to DM2, are two factors that are related and could themselves have an impact on CVD.

2.1.1 Dyslipidemia

Dyslipidemia is one of the major cardiovascular risk factors (Kopin *et al*., 2017). It is characterized by increased levels of triglycerides (TG) and/or low-density lipoproteins (LDL), in addition to decreased levels of high-density lipoproteins (HDL). (Lui & Li, 2014). In Mexico, the most common dyslipidemia is increased triglycerides known as hypertriglyceridemia. In the last National Health and Nutrition Survey (ENSANUT) it was reported that 57.5% of the population had triglyceride levels above 150 mg/dL. (National Institute of Public Health, 2019).

2.1.2 Hypertriglyceridemia

Hypertriglyceridemia (HTG) is a common abnormality of lipid metabolism (Pedragosa, et al 2013). It is often clinically silent and is most frequently found during screening of patients without any symptoms. According to the most recent clinical guidelines, triglyceride levels are considered normal if they are less than 150 mg/dL, borderline high if 150 to 199 mg/dL, high if 200 to 499 mg/dL, and very high if 500 mg/dL or higher. (Elkins & Friedich, 2018).

It is a disorder usually accompanied by other lipid profile alterations and is currently a cardiovascular risk factor that should be investigated in at-risk individuals. Early detection of high plasma triglyceride concentrations in children, adolescents and young adults is of paramount importance to prevent future cardiovascular events (González-Sandoval *et al*., 2014). Recent evidence suggests that this pathology is strongly associated with an insulin resistance (IR) profile, since it favors lipogenesis and there tends to be an elevation of plasma triglyceride levels (Fiuza *et al*., 2018). The mechanisms by which this situation occurs have been empirically demonstrated and encourage further research into both pathologies.

2.1.3 Insulin resistance

Insulin resistance (IR) is a metabolic disorder characterized by an attenuated biological response to the action of insulin. It is defined as a state in which an increased amount of insulin is required to produce a normal biological response to a glucose load, i.e., compensatory hyperinsulinism develops. (Centers for Disease Control and Prevention, 2017).

The development of IR is influenced by genetic and environmental factors, such as a high-trans-fat, high-calorie diet, obesity, ageing and sedentary lifestyle. It results in decreased glucose uptake by skeletal muscle and adipose tissue cells, decreased hepatic glycogen production (glycogenolysis) and increased hepatic glucose production (glycogenolysis) (Martínez Basila *et al.* 2011).

The standard method to identify IR is the hyperglycemic clamp method, however, due to its high cost and difficulty to perform, the HOMA index has been proposed as a suitable model to assess and determine IR at an affordable cost.

2.1.4 HOMA Index

The Homeostasis Model Assessment (HOMA) index was proposed by Mathews et al in 1985. It is the most widely used method for diagnosing IR in humans and was derived from a mathematical equation relating β-pancreatic cell function and fasting glucose and insulin concentrations. The equation is calibrated with a β-cell function assumed to be 100% and with a normal RI of 1 (Martinez-Basila *et al.*, 2011) according to the following formula:

Figure 1.1 Insulin resistance HOMA formula

$$HOMA-IR=\frac{\text{insulina } plasmática \text{ en ayuno (mU/L)}\times\text{glucosa plasmática en ayuno (mmol/L)}}{22.5}$$

Source: Martínez, 2011

The HOMA index can also be used to assess β-pancreatic cell function. Thus, the HOMA model is used to estimate insulin sensitivity and β-cell function. This is because plasma insulin and glucose concentrations have a relationship in the basal state and reflect the balance between hepatic glucose and insulin secretion that is maintained by feedback between the liver and β-cells (Wallace *et al*., 2004).

HOMA index values in a population of Mexican descent are considered normal when they are less than 2.60. However, values between 2.60 and 3.80 refer to moderate IR, while values above 3.80 represent severe IR (Qu et al. 2011). The growing increase in metabolic diseases such as those mentioned above, especially in the young population, has increased interest in studying this population and the possible factors that could influence the development of these diseases.

University students have been specifically singled out as a population of interest for reasons such as age, educational level, lifestyles associated with long hours of study and class attendance, among others. Students from the health field, have the potential, soon, to apply their knowledge in society (Maldonado et al, 2013).

Students are subjected to conditions when entering the university system. They are at a critical stage in the development of their eating habits, characterized by little time to eat, frequent skipping of meals, eating between meals, high consumption of fast food, among others. In addition to this, there is a decrease in physical activity due to the rise of passive entertainment. Furthermore, there has been an increase in the prevalence of tobacco and alcohol consumption. These unhealthy lifestyles are contributing to the development of cardio-metabolic risk factors in university students (Kim & Park, 2016)

There is a high prevalence of risk factors for chronic non-communicable diseases in university students, including overweight and obesity, insulin resistance especially in women and hypertriglyceridemia in men (Morales, 2013). Early identification of possible modifiable risk factors for cardio-metabolic diseases is of vital importance for their early prevention. Therefore, the aim of this study was to look for the possible association between two risk factors such as hypertriglyceridemia and insulin resistance as a possible predictor of cardio-metabolic risk.

2.2 Materials and Methods

Students from the Centro Universitario de Ciencias Exactas e Ingenierías of the University of Guadalajara, Mexico, with the following characteristics was recruit: aged between 18 and 25, with 10 to 12 hours of fasting, were recruited for this study. They attended to the Biochemistry Laboratory, where personal data was registered, a clinical history was filled out and somatometric measurements were obtained. At the end, a blood sample was taken.

Transversal analytic study type. The next parameters were determined.

- Body Mass Index. Weight and height were measured using a TANITA30A scale that automatically calculates the BMI, which was used to characterize the population as normal weight, overweight and obese, considering: 19 - 24.9 kg/m^2, 25 - 29.9 kg/m^2 and ≥ 30 kg/m^2 BMI, respectively.

- Serum analysis of total cholesterol (TC), triglycerides and glucose were measurement using a dry chemist technique in the FujiFilm DriChem NX500i equipment. LDL was calculate using Friedwald formula.

- The determination of insulin was using a ELISA sandwich type technique in the Magpi Luminex equipment. A cut off point of >150 mg/dL was considered for hypertriglyceridemia and for insulin resistance HOMA index > 2.5 was used.

2.3 Results

We recruit a total of 189 students, 61% of whom were female and the rest male. Table 2.1 shows the general characteristics obtained, separated by gender, and the percentage of students with alterations in triglycerides and insulin resistance.

Table 2.1 Descriptive anthropometric and biochemical results

Variable	Women n= 116	Men n= 73	Impaired (%)
Age (years)	20.52 ± 1.44	21.0 ± 1.91	
BMI (Kg/m^2)	24.8 ± 5.26	28.11 ± 6.48	%67 (127)
Total Cholesterol (mg/dL)	168.5 ± 34.57	162.34 ± 34.30	
Triglycerides (mg/dL)	**97.99 ± 51.03**	**112.90 ± 55.36**	**%17 (33)**
HDL (mg/dL)	50.13 ± 13.03	40.3 ± 9.18	
LDL (mg/dL)	99.61 ± 26.06	95.14 ± 38.47	
Glucose (mg/dL)	83.61 ± 7.99	85.55 ± 8.82	
Insulin (mU/L)	10.28 ± 0.44	12.51 ± 9.62	
HOMA (mU*mmol/L^2)	**2.06 ±1.54**	**2.55 ± 1.86**	**%30 (57)**

Table 2.1 shows that the results are within normal parameters, except for the BMI in men, which is on average in the overweight range. It can also be seen that men have the highest HOMA levels, slightly above the normal range. A prevalence of hypertriglyceridemia of 17% was found in our population. 34% of which were women, the rest men. Insulin resistance was diagnosed in 57 volunteers, which corresponds to a prevalence of 30%. Of these, 49% were female. In addition, 9.5% had both disorders.

The association between IR and hypertriglyceridemia was performed. An Odds Ratio (OR) of 3.890 $p<0.0004$ (CI 1.771-8.545) was obtained. This result shows that the presence of elevated triglyceride levels can be considered per se a cardio-metabolic risk factor, since it increases the likelihood of insulin resistance to a great extent, that along with these two factors, represent an increased risk of these diseases.

2.4 Discussion

The relevance of this study lies in the population being studied, although these are apparently healthy young university students, the frequency of dyslipidemias was observed to be high. In addition, a correlation was found between plasma triglyceride values and the HOMA index of insulin resistance in non-diabetic males. Fasting hypertriglyceridemia is an abnormality commonly found in insulin-resistant subjects and is frequently associated with other elements of insulin-resistant dyslipidemia.

There are explanations for this close association, as mechanisms have been demonstrated by which insulin resistance leads to hypertriglyceridemia and there are also mechanisms by which the degree of insulin resistance increases. Visceral adipocytes are generally more insulin resistant, so they show marked lipolysis and an increased flow of fatty acids to the liver. The increase in fatty acids has two consequences in the liver: firstly, it increases the synthesis of triglycerides and secondly, it favors the synthesis of very low-density lipoproteins (VLDL) that pass into the blood in large quantities and cause hypertriglyceridemia (Miguel Soca *et al*., 2011).

The increase in triglycerides in the blood is possibly due to a decrease in the clearance of VLDL, triglyceride-rich lipoproteins that are removed from the circulation by an endothelial enzyme, whose activity depends on insulin and is reduced in insulin resistance. Hypertriglyceridemia affects the lipoprotein pattern by promoting lipid exchange between VLDL and high-density lipoproteins (HDL), through the action of cholesteryl ester transfer protein. In this exchange, triglycerides are transferred to HDL and cholesteryl esters to VLDL, enriching the triglyceride content of HDL and increasing the cholesterol content of VLDL. Triglyceride-rich HDL are more susceptible to degradation by hepatic lipase, which reduces their blood concentrations and affects the role of these lipoproteins in reverse cholesterol transport, the main cardio-protective mechanism of HDL (Tilg *et al*., 2008).

Resistance to insulin action (decreased response to the hormone) in skeletal muscle is one of the first detectable defects in humans with type 2 diabetes. Obesity is the most important risk factor for the development of this pathology and specifically central fat deposits (visceral obesity). Initially, insulin resistance generates compensatory mechanisms so that, for a certain period, insulin hypersecretion keeps blood glucose levels under control. This period, which could be called pre-diabetic, is difficult to detect because blood glucose levels remain within normal limits. However, this situation deteriorates until pancreatic failure occurs, which is when the beta cells are no longer able to maintain insulin hypersecretion, begin to deteriorate and this deterioration leads to reduced insulin secretion. This is the point at which most cases of type 2 diabetes mellitus and metabolic syndrome start to be diagnosed (Genoni *et al*., 2017).

The progression of insulin resistance not only leads to type 2 diabetes, but if appropriate measures are not taken, patients will become insulin dependent. Although the etiology of resistance is not yet clearly established, it is thought that there is a polygenic genetic component that is mediated by the environment. In this sense, the lifestyle with little physical exercise and constant availability of food, which is the case in our society, seems to be responsible for the escalation in recent years in the incidence of insulin resistance related diseases. More than 90% of diabetics are classified as type 2. According to the World Health Organization, the number of people worldwide affected by this disease has tripled in the last 20 years. Forecasts for the not-too-distant future are that almost 30% of the population will develop insulin resistance and its complications during their lifetime (Benito M., 2014).

Insulin resistance is associated with hyperinsulinemia, hypertension, dyslipidemia, and is a risk factor for cardiovascular disease, including in children. It is for this reason that the diagnosis of young people with insulin resistance has been proposed as a strategy to identify those at high risk of becoming diabetic (Haymond, 2003), since in the pathophysiology of type 2 diabetes mellitus, the first step is the presence of insulin resistance.

Insulin resistance and the so-called metabolic syndrome where hypertriglyceridemia is implicated as a primary factor, are constituted as two complex pathological entities, which represent a real challenge for clinicians and specialists in terms of their proper definition and diagnosis. Even today, with advanced technological resources and well-established clinical principles, it is necessary to continue the research into the pathophysiological mechanisms and the most effective and safe therapeutic approaches to these entities.

The basis of these primary prevention measures, so far, continues to be lifestyle modifications (weight reduction, low-calorie diet, and exercise); in addition, an individual assessment should be performed in populations at higher risk (family history of diabetes, macrocosmic product, central obesity, arterial hypertension, glucose intolerance and hypertriglyceridemia and some other early markers) that may lead to the presence of hyperinsulinemia and metabolic syndrome. The presence of both hypertriglyceridemia and insulin resistance, and their probable complications, in all population groups compromises the present and future health of people, which is why it is considered a public health problem and therefore requires the attention not only of health professionals but also of the economic and political authorities of our entity.

2.5 Conclusions

- Higher BMI, triglyceride, glucose, insulin and HOMA values were observed in males.

- Similarly, females have a lower prevalence of hypertriglyceridemia. However, they are almost equally prevalent as the male gender in terms of insulin resistance.

- With these data, we can conclude that hypertriglyceridemia can indeed be associated with insulin resistance. The volunteers were young students, reason for which it is necessary to insist on a lifestyle improvement, because despite their young age, some severe disorders have been observed, which will have repercussions in their adult life.

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2.7 Conflicts of interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this document.

2.8 References

Baeradeh, N., Ghoddusi Johari, M., Moftakhar, L. et al. The prevalence and predictors of cardiovascular diseases in Kherameh cohort study: a population-based study on 10,663 people in southern Iran. BMC Cardiovasc Disord 22, 244 (2022). doi.org/10.1186/s12872-022-02683-w. https://bmccardiovascdisord.biomedcentral.com/articles/10.1186/s12872-022-02683-w#citeas

Benito M. 2014. Patologías asociadas a la obesidad. Síndrome metabólico y diabetes melitus tipo 2. En Primer curso Avanzado sobre Obesidad (eds M Cascales, F Sánchez Muniz y B Ribas). Monografía XXXVIII de la RANF. Madrid. pp 128 – 148.

Centers for Disease Control and Prevention. 2017 *National Diabetes Statistics Report*. Atlanta, GA: Centers for Disease Control and Prevention, US Department of Health and Human Services; 2017. URL: https://www.cdc.gov/diabetes/data/statistics-report/index.html.

Elkins C, Friedrich D. 2018 "Hypertriglyceridemia: A review of the evidence". *Nurse Pract.* Oct;43(10):22-29. doi: 10.1097/01.NPR.0000544997.22887.0b. https://pubmed.ncbi.nlm.nih.gov/30153192/

Fiuza-Luces C, Santos-Lozano A, Joyner M, Carrera-Bastos P, Picazo O, Zugaza JL, Izquierdo M, Ruilope LM, Lucia A. 2018. "Exercise benefits in cardiovascular disease: beyond attenuation of traditional risk factors". *Nat Rev Cardiol.*Dec;15(12):731-743. doi: 10.1038/s41569-018-0065-1. https://pubmed.ncbi.nlm.nih.gov/30115967/

Genoni G, Menengon V, Secco G, Sonzini M, Martelli M, Castagno M, et.al. Insulin resistance, serum uric acid and metabolic syndrome are linked to cardiovascular dysfunction in pediatric obesity. Int J Cardiol. 2017; 249::366-371. DOI: 10.1016/j. ijcard.2017.09.031. URL: https://pubmed.ncbi.nlm.nih.gov/28935462/

González Sandoval, Claudia Elena, Díaz Burke, Yolanda, Mendizabal-Ruiz, Adriana Patricia, Medina Díaz, Eunice, & Morales, José Alejandro. (2014). Prevalencia de obesidad y perfil lipídico alterado en jóvenes universitarios. Nutrición Hospitalaria, 29(2), 315-321. https://dx.doi.org/10.3305/nh.2014.29.2.7054. URL: http://scielo.isciii.es/scielo.php?script=sci_arttext&pid=S0212-16112014000200010&lng=es

Haymond M. 2003. "Measuring insulin resistance: a task worth doing but how? Pediatr Diabetes". 4(3):115-118. DOI: https://doi.org/10.1034/j.1399-5448.2003.00024.x. URL https://pubmed.ncbi.nlm.nih.gov/14655268/

Joseph P, Leong D, McKee M, Anand SS, Schwalm JD, Teo K, Mente A, Yusuf S. 2017 "Reducing the Global Burden of Cardiovascular Disease, Part 1: The Epidemiology and Risk Factors". *Circ Res*. Sep 1;121(6):677-694. doi: 10.1161/CIRCRESAHA.117.308903. URL: https://pubmed.ncbi.nlm.nih.gov/28860318/

Kim JH, Park YS. 2016. "Low muscle mass is associated with metabolic syndrome in Korean adolescents: the Korea National Health and Nutrition Examination Survey 2009-2011". *Nutr Res.* 36(12):1423-28 doi:10.1016/j.nutres.2016.09.013. URL: https://pubmed.ncbi.nlm.nih.gov/27884414/

Kopin L, Lowenstein C. 2017. "Dyslipidemia". *Ann Intern Med.* Dec 5;167(11): ITC81-ITC96. doi: 10.7326/AITC201712050. URL: https://pubmed.ncbi.nlm.nih.gov/29204622/

Liu HH, Li JJ. 2015. "Aging and dyslipidemia: a review of potential mechanisms". *Ageing Res Rev.* 2015 Jan; 19:43-52. doi: 10.1016/j.arr.2014.12.001. URL: https://pubmed.ncbi.nlm.nih.gov/25500366/

Maldonado Villalón JA, Carranza Cervantes CA, Ortiz González MJ, Gómez Alonso Carlo, Cortés-Gallegos NL. Prevalencia de factores de riesgo cardiometabólico en estudiantes universitarios de la región centro-occidente, en la Universidad Michoacana de San Nicolás de Hidalgo, México. (2013). 24 (2) pp 76-86.

Martínez Basila A, Maldonado Hernández J, López Alarcón M., 2011. "Métodos diagnósticos de la resistencia a la insulina en la población pediátrica". Boletín Médico del Hospital Infantil de México. 68(5) 397-404.

Miguel Soca PE, Cruz Torres W, González Ferrer J, Cardona Cáceres X, Cruz Lage LA, Hernández Tamayo M. 2011. "Efectos beneficiosos de cambios en la dieta y ejercicios físicos en mujeres obesas con síndrome metabólico". *Revista Panorama Cuba y Salud*: http://www.panorama.sld.cu/pdf/publicaciones_a nteriores/v_4no_3/dieta.pdf

Morales I, Gladys, del Valle R, Carlos, Soto V, Álvaro, & Ivanovic M, Daniza. 2013. “Factores de riesgo cardiovascular en estudiantes universitarios”. *Revista chilena de nutrición*, 40(4), 391-396. https://dx.doi.org/10.4067/S0717-75182013000400010

National Institute of Public Health. 2019. National Survey of Health & Nutrition 2018. Secretaría de Salud Pública. https://ensanut.insp.mx/encuestas/ensanut2018/doctos/informes/ensanut_2018

Pan American Health Organization, 2017. Cardiovascular Diseases Program. Pan American Health Organization.URL:https://www.paho.org/hq/index.php?option=com_content&view=article&id=1939:cardiovascular-diseases-program-home&Itemid=1819&lang=es

Pedragosa Àngels, Merino Jordi, Aranda Arcas José Luis, Galiana Jesús, Godoy Diego, Josefa María Panisello Royo, Juan Francisco Ascaso Gimilio, Fernando Civeira Murillo, Lluís Masana Marín, Juan Pedro-Botet Montoya 2013. “Perfil clínico de los pacientes con hipertrigliceridemia muy severa del Registro de Hipertrigliceridemias de la Sociedad Española de Arteriosclerosis” *Clínica e investigación en arteriosclerosis*, ISSN 1578-1879, Vol. 25, Nº. 1, 2013, págs. 8-15. DOI: 10.1016/j.arteri.2012.11.001. https://www.elsevier.es/es-revista-clinica-e-investigacion-arteriosclerosis-15-articulo-perfil-clinico-pacientes-con-hipertrigliceridemia.

Qu HQ, Li Q, Rentfro AR, Fisher-Hoch SP, McCormick JB. The definition of insulin resistance using HOMA-IR for Americans of Mexican descent using machine learning. PLoS One. 2011;6(6):e21041. doi: 10.1371/journal.pone.0021041. https://pubmed.ncbi.nlm.nih.gov/21695082/

Tilg H, Moschen AR. Inflammatory mechanisms in the regulation of insulin resistance. Mol Med. 2008 Mar-Apr;14(3-4):222-31. doi: 10.2119/2007-00119. URL: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2215762/

Wallace T.M., Levy J.C., Matthews D.R. 2004. *Use and abuse of HOMA modeling*. Diabetes Care. 27:87-95. doi: 10.2337/diacare.27.6.1487. URL: https://pubmed.ncbi.nlm.nih.gov/15161807/

Weschenfelder C, Schaan de Quadros A, Lorenzon Dos Santos J, Bueno Garofallo, S,Marcadenti, 2020. “Adipokines and Adipose Tissue-Related Metabolites, Nuts and, Cardiovascular Disease”. *Metabolites*. Jan 11;10(1). pii: E32. doi: 10.3390/metabo10010032 URL https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7022531/

World Health Organization. 2017. Cardiovascular diseases. World Health Organization. https://www.who.int/es/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds)

Wu Y, Ding Y, Tanaka Y, Zhang W. Risk factors contributing to type 2 diabetes and recent advances in the treatment and prevention. Int J Med Sci. 2014 Sep 6;11(11):1185-200. doi: 10.7150/ijms.10001. URL. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4166864/