

Is there association between dislipidemia and diabetes type 2 in the population of Castilla-La Mancha?

David Oliver Tébar*

Investigator of the Department of Medical Sciences, Faculty of Medicine of Albacete, UCLM - Spain

Abstract

Background and objective: The dislipidemia is one of the main factors of risk of cardiovascular illness in patients with diabetes mellitus type 2 (DM2). The aim of this study is to evaluate the prevalence and factors of risk associated to the dislipidemia in the population with DM2 of the Community of Castile-La Mancha.

Material and methods: It is a longitudinal study made in centres of Attention Primaria of the Service of Health of Castilla-La Mancha (n = 70). It selected a representative sample of the population with DM2 of 18 to 85 years by means of a procedure polietápico. They obtained of the clinical history and by means of interview the data of the factors of risk to study. It analysed the association with the dislipidemia by means of linear regression.

Results: 52,1% were men, the half age was of 69,8 years, the evolution of the diabetes of 9,99 years, 84,3% had HTA, 76,6% sobrepeso/obesigive and the HbA1c half was of 6,96%. The prevalence of dislipidemia was of 85,3% and in the analysis bivariado associated with antecedent of peripheral vascular illness, diabetes controlled, treatment antihipertensivo, filtered glomerular, HbA1c > 7%, grasto corporal estimated in sobrepeso and obesity, antecedent of cardiovascular illness, age and HbA1c. In the univariant analysis the independent factors were the feminine sex and the antecedent of cardiovascular illness.

Conclusions: The prevalence of dislipidemia in our study was of 85,3%. The factors of risk associated of independent form were the feminine sex and the personal antecedent of cardiovascular illness.

Introduction

The diabetes mellitus type 2 (DM2) is an illness that has purchased a character pandémico because of the increase of the hope of life, that supposes an increase of the aging of the population, to the increase of the obesity and to the change in the lifestyles to some habits no cardiosaludables (sedentarism and bad feeding) [1].

The prevalence of DM2, according to the study di@bet.es, emplaza in 13,79% of the Spanish population elder of age. According to data of the Organisation Mundial of the Health (2016), in Spain the DM finds between the causes of death more frequent. The proportional mortality that attributes to this illness is of 3% of the total of deaths for all the groups etarios.

The DM comports notable costs socioeconómicos. Crespo Et al. They signalled that, in 2013, the annual cost of the DM was of 5. 890 million euros: 8,2% of the sanitary cost total [2].

In the patients with diabetes, the complications microvasculares are the main cause of morbimortalidad to level mundial. Near of 3/4 parts die by cardiac illness or cerebrovascular. Likewise, the frequency of deaths by cardiovascular reasons in adults diabéticos in comparison with the no diabéticos is of 2 to 4 greater times [3]. The importance of the quilomicrones for the reduction of the cardiovascular risk in the DM2 has been showed in different studies and metaanálisis [4]. The association between dislipidemia and cardiovascular illness (ECV) remained showed in the "United Kingdom Prospective Diabetes Study (UKPDS 23)", where observed that an increase of 38,5 mg/dl in the concentration of quilomicrones associates to an increase of 157% to present coronary arterial illness and that an increase of 4 mg/dl of the cHDL associates to a descent of 15% of events cardiovasculares [3]; like

this then, the factor of risk of greater weight to develop coronary illness were the quilomicrones, followed of the levels of cHDL. It is necessary to diagnose and treat tempranamente the dislipidemia of effective form for like this reduce the risk of cardiovascular events futures [1].

In Spain, diverse studies epidemiológicos have analysed the prevalence of the alterations lipídicas, that oscilate between 56,2% in the one of Domínguez and 92,6% in the study OBEDIA8; however, it is scarce the information on the prevalence and the factors associated to the dislipidemia in patients with DM2 in Castile-La Mancha [5].

The present study has like aims: 1) estimate the prevalence of the dislipidemia; 2) investigate the factors of risk associated to the dislipidemia and 3) investigate the factors of risk associated of independent form to the dislipidemia.

Material and methods

Longitudinal study of populational base on a sample of 70 patients with DM2, between November of the 2019 and February of the 2020. It made a procedure polietápico by means of the employment of a sample of the conglomerates of some centres of health. Of the 60 centres of health registered in the Service of Castile-La Mancha of Health, selected 30. The greater part of this in the province of Albacete (where selected

*Correspondence to: David Oliver Tébar, Investigator of the Department of Medical Sciences, Faculty of Medicine of Albacete, UCLM, Spain, E-mail: dlotebar@gmail.com

Key words: dislipidemia, diabetes mellitus type 2, prevalence, factors of risk

Received: April 20, 2020; **Accepted:** May 15, 2020; **Published:** May 18, 2020

20), in Cuenca selected 4, in Ciudad Real 3 and in Toledo other 3. Later there was a second selection of a submuestra of the contingents of patients of the doctors of each centre of health elegido. If any of the centres of health rejected to participate in the study, was replaced by another inside the same stratum.

Of each included patient in the study collected information of the following variables: age, sex, year of diagnostic of DM2, habitat, level of education, familiar economic level, labour situation, habit tabáquico, weight, size, perimeter abdominal waist, corporal fat estimated, index of corporal mass (IMC), arterial pressure sistólica, arterial pressure diastólica, abdominal obesity, antecedents of ECV, arterial hypertension (HTA), treatment antihipertensivo, dislipidemia, treatment hipolipidemiante, renal insufficiency and retinopathy.

Besides, they collected the analytical parameters of quotient albumin/creatinina, filtered glomerular (FG), hemoglobin glicosilada (HbA1c), glucemia plasmática, total cholesterol (CT), cLDL, cHDL, triglycerides (TG) and creatinina. For the register of the presartrial ion made 2 measurements of arterial pressure sistólica and diastólica in 2 successive visits and with monitor of arterial pressure validated. For the analysis used the average of the 2 measurements.

For the analysis of data used the programa statistician SPSS V23.0.0.0. The qualitative variables expressed like absolute value and percentage, with the estimate of the interval of confidence to 90% (IC 90%). The quantitative variables expressed like half \pm typical deviation and IC 90%. For the relation of the quantitative and qualitative variables between himself employed an analysis bivariado with t of Student. It made the analysis multivariado of binary linear regression no conditional with the dislipidemia like dependent variable, having in cuenta the variables that in the analysis bivariado associated with the presence of the dislipidemia or were clinically notable, that were the following: age, sex, HTA, personal antecedent of peripheral vascular illness, diabetes controlled, treatment antidiabético, HbA1c \geq 7%, quotient albumin/creatinina, FG, personal antecedent of ECV, years of evolution of DM, glucemia basal, creatinina and retinopathy. All the statistical analyses were of 1 tail and considered estadísticamente significativo a value of $< p$ 0,05.

Results

Of the 70 patients, 68,9% were 65 years old or more, with average of age of 69,84 years and average of years of evolution of the diabetes of 9,99 years. 68,2% of the participants were of urban habitat, 50% had primary studies, 74% were jubilados and 75% had annual income $<$ 18.000 D. There was a light predominance of men (52,1%) and the women were of greater age (70,8 years). The tabaquismo active and the obesity according to the IMC was significantly greater in men; the abdominal obesity was significativamente greater in women. The prevalencia of dislipidemia was of 85,3%; the one of HTA, of 84,3%; renal insufficiency, of 22,9%; sedentarism, of 48,2%; oligoalbuminuria and proteinuria, 31,3%; sobrepeso and obesity according to IMC, of 76,6%; obesity according to the corporal fat estimated by means of CUN-BAE, of 93%; abdominal obesity, of 67,6% and the retinopathy was of 29,3%. The prevalencia of dislipidemia was similar in women and men (87,7% in women in front of 83,1% in men; $p = 0,085$). Of the subjects dislipidémicos, 79,5% were dislipidémicos for receiving treatment hipolipidemiante and 20,5%, dislipidémicos that did not receive treatment hipolipidemiante and that presented values of cLDL $>$ 160 mg/dl, cHDL $<$ 40 mg/dl in men or $<$ 50 mg/dl in women, or TG \geq 150 mg/dl. The 75,3% received treatment hipolipidemiante; 71,1%, estatinas; 5,4%, ezetimiba; 3,3%, fibratos; 0,8%, resins of ionic

exchange and 0,5%, esters etílicos of sour grasos omega 3. 69,6% received treatment in monoterapia and 5,7% in biterapia. In the subjects dislipidémicos for receiving treatment hipolipidemiante, 96,5% received estatinas or ezetimiba; 4,3%, fibratos and 2%, estatinas and fibratos. In the subjects with diagnostic of dislipidemia and without treatment hipolipidemiante, the 14,3% had the cLDL $>$ 160 mg/dl; 79%, cHDL $<$ 40 mg/dl in men or $<$ 50 mg/dl in women and 51,3% had TG $>$ 150 mg/dl. The average of glucemia plasmática basal was of 137,85 \pm 46,59 mg/dl, of CT 178,17 \pm 38,18 mg/dl, of cHDL 47,09 \pm 12,10 mg/dl, of cLDL 108,10 \pm 36,44 mg/dl, of TG 136,6 \pm 66,3 mg/dl and of creatinina 0,96 \pm 0,55 mg/dl.

68,7% of the patients had normoalbuminuria; 23,8%, oligoalbuminuria and 7,5%, self-evident proteinuria. 77,1% of the patients had a tax of filtered glomerular (MDRD) TFGe $>$ 60 ml/min/1,73 m² and 22,9%, renal insufficiency (TFGe $<$ 60 ml/min/1,73 m²). Of the patients with renal insufficiency, 19,1% had TFGe of 30-59 ml/min/1,73 m²; 2,9%, of 15-29 ml/min/1,73 m² and 0,9%, $<$ 15 ml/min/1,73 m². The average of glucemia plasmática basal, TG and creatinina was significantly greater in men and, the average of CT, cHDL and cLDL was significantly greater in the women. To his time, the oligoalbuminuria and proteinuria was significantly more prevalent in the men. They obtained the parameters lipídicos complete of 70 patients that had registered one or more parameters. Of them, 26,6% did not reach the aims of CT ($<$ 200 mg/dl) neither 54,9% the ones of cLDL ($<$ 100 mg/dl). They documented TG high (\geq 150 mg/dl) in 33,7% and cHDL low ($<$ 40 mg/dl in men and $<$ 50 mg/dl in women) in 46%. With regard to the alterations combined, cLDL out of aims and cHDL low detected in 23,7%; cLDL out of aims, cHDL low or TG elevated in 14% and cLDL and CT fuerto of aims, cHDL low or TG elevated in 6,6%. In the analysis bivariado, the variables associated to the presence of dislipidemia are: antecedent of peripheral vascular illness, diabetes controlled, farmacological treatment for HTA, HbA1c \geq 7%, FG, corporal fat estimated in sobrepeso and obesity, personal antecedent of ECV, age and HbA1c (Table 1). The antecedent of peripheral vascular illness is included in the variable antecedent of ECV.

We have not found significant differences in the presence of dislipidemia with the following variables: sex, familiar economic level, level of education, labour situation, habitat, habit tabáquico, HTA, HTA controlled, farmacological treatment DM, quotient albumin/creatinina, IMC, obesity abdominal, retinopathy diabética, years of evolution, glucemia basal neither creatinina. In spite of have not found significant differences, objetivamos that the subjects with dislipidemia had greater time of evolution of his DM, greater levels of glucemia basal and dand creatinina and greater values of IMC. To his time, the feminine sex, the black race, the familiar economic level «annual incomes $<$ 18.000 D», the low level of education (without studies and primary studies), the labour situation «jubilado» and the urban habitat fueron more prevalentes in the subjects dislipidémicos. Likewise, the habit tabáquico (smoker and exfumador), the HTA, the oligoalbuminuria, the proteinuria and the retinopathy diabética were more prevalentes in pacientes dislipidémicos that in no dislipidémicos. También objetivó That the prevalencia of the dislipidemia was elder to measure that increased the oligoalbuminuria and the degree of retinopathy diabética, as well as, when the TFGe diminished.

In the analysis multivariable, identify that the variables that asocian of independent form with the dislipidemia are: the feminine sex and the personal antecedent of ECV (Table 2).

Table 1. Quantitative variables associated to the presence of dislipidemia. Clinical diagnostics of dislipidemia*

Variables	No dislipidemia +/- OF	Dislipidemia Current +/- OF	p	OR Raw	IC 95%
Age (years)	67,54 +/- 14,75	70,63 +/- 11,48	0,018	1,02	(1,00-1,04)
Years of evolution DM (years)	9,17 +/- 3,98	10,13 +/- 4,70	0,054	1,05	(0,99-1,10)
HbA1c (%)	6,70 +/- 1,40	7,01 +/- 1,34	0,030	1,23	(1,02-1,49)
Glucemia Basal (mg/dl)	132 +/- 50	139 +/-46	0,178	1,00	(0,99-1,01)
CT (mg/dl)	186 +/- 30	177 +/- 39	0,024	0,99	(0,98-0,99)
LDL (mg/dl)	111 +/- 25	108 +/- 41	0,464	0,99	(0,99-1,00)
HDL (mg/dl)	56 +/- 12	46 +/- 14	0,000	0,95	(0,94-0,97)
TG (mg/dl)	90,21 +/- 30,75	145,83 +/- 72,64	0,000	1,02	(1,01-1,03)
Creatinina (mg/dl)	0,87 +/- 0,44	0,98 +/- 0,57	0,068	1,78	(0,96-3,32)

***Dislipidemia:** In treatment hipolipidemiante or those that do not follow treatment hipolipidemiante and present figures of cLDL > 160 mg/dl; cHDL < 40 mg/dl in men and <50 mg/dl in women or TG > 150 mg/dl. cHDL: Cholesterol joined to lipoproteins of high densidad, cLDL: cholesterol joined to lipoproteins of low density, CT: Total Cholesterol, DM: Diabetes Mellitus, HbA1c: Hemoglobin Glicosilada, IC: Interval of Confidence, OR: *odds ratio*, TG: Triglycerides.

Table 2. Model multivariado. Variables associated of independent form with the dislipidemia

Variables	B	EE	p	OR	IC 95%
Sex (M vs. H)	1,028	0,273	0,000	2,79	1,64-4,78
Personal antecedents of ECV	1,253	0,329	0,000	3,50	1,84-6,66
HbA1c greater or the same to 7%	0,531	0,283	0,060	1,70	0,98-2,96
Age	0,015	0,010	0,137	1,02	0,99-1,04
Constante	0,381	1,009	0,706	1,46	

The model contains the following variables: sex (woman vs. man), personal antecedents of ECV (ictus, cardiopathy isquémica and arteriopatía peripheral), HbA1c>7% and age (continuous, by every year of more).

B: Coefficient of Regression, ECV: Cardiovascular Illness, EE: Standard Error of B, H: Men, HbA1c: Hemoglobin Glicosilada, IC: Interval of Confidence, M: Women, OR: *odds ratio*.

Discussion

The results indicate that the prevalencia of dislipidemia in patients with DM2 of Castile-La Mancha is elevated and that less than 15% of the patients show the values lipídicos normal or recommended by the main guides of clinical practice. Said findings of prevalencia are consistent with the found in other works so much in Spain as in the international field. When we compare these results with different publications, observe that it exists a big variabilidad. In the majority of the studies the prevalencia of dislipidemia finds above 50%, with a rank that oscillates between 56,2% in the one of Domínguez and 92,6% in the study OBEDIA. On the other hand, the variability found in the prevalencia of dislipidemia can be due to the heterogeneity in the form to diagnose it and to that is in relation with the different criteria diagnostics. In this context, the greater prevalencia observed in the study OBEDIA could be in relation with the point of court of the cLDL considered in the definition of dislipidemia, that is lower than the used in the present study. These discrepancies are something usual in the medical bibliography, since the methodologies used to the hour to carry out the studies (is possible that other studies use distinct criteria diagnostics, methods of laboratory or different points of cut to determine the diverse factors lipídicos and his cardiovascular risk), as well as the populational diversity, affect to the resultados ends of the studies. Also it is important recalcar that the studies from populational samples can have the inconvenient that, in spite of his aleatoriedad in the selection of the subjects, the sample do not represent the population of reference or that this find very delimited in the space and the time and, therefore, was not comparable with other studies. This prevalencia so high could be related with the profile of the patients studied (high taxes of obesity, enfermrenal age, bad metabolic control of the diabetes, etc.), since in the sample studied 69% were greater of 65 years. These analytical values do not depend of the register made by the professionals and are a faithful reflection of the reality.-Although in multiple studies epidemiológicos longitudinal has analysed the prevalency of dislipidemia in poblaciones diabéticas with distinct levels of cardiovascular risk, east is the first study in Spain that analyses the characteristics, prevalencia and factors associated to the dislipidemia of

a representative sample of pacientes with DM2 of Castile-La Mancha. Besides, the previous studies to the moment to value the prevalencia of dislipidemia centre usually in the isolated alteration of the CT or cLDL according to the recommendations of the NCEP ATP III, without a complete analysis of the profile lipídico and without taking into account to patients in treatment hipolipidemiante.

In the subjects with diagnostic of dislipidemia and without treatment hipolipidemiante objetivamos that the low values of cHDL is the alteration lipídica more frequent (79%). Of the same way, observe a considerable increase of the levels of TG (51,3%) beside a discreet increase of the values of cLDL (14,3%). These results are concordantes with the quantitative alterations described in the dislipidemia in the patient with DM «dislipidemia aterogénica». The dislipidemia aterogénica is a characteristic element of the vascular residual risk of origin lipídico no associated to changes in the neithergo them of cLDL and is a dislipidemia very prevalente in the people with DM2, in the patients with high risk or very high risk, with visceral obesity or metabolic syndrome.

In the sample studied observes that a high proportion of patients no alcanzan the aims of cLDL. Also objetivamos that an important proportion of cases has TG high and cHDL low, which saves concordance with the described in the bibliography, where finds elevation of the TG and decrease of the cHDL in aproximatemind the half of the patients with DM2. These data signal an important residual risk (levels of cLDL, cHDL and TG subóptimos) that probably have to be controlled with more intensity of what does in the daily clinical practice and that perhaps was in relation with the inertia and therapeutic fulfillment; in patients with DM2, the percentage of incumplimiento therapeutic is very high, and is of the 32, 36 and 38% for the hipolipidemiantes, antidiabéticos and antihipertensivos. If we examine the fulfillment of objetivos according to the recommendations of the guides of clinical practice, objetivamos that the 2/3 parts of the subjects have suitable levels of TG (67,2%) and less than the half do not reach the optimum levels of cLDL (45,1%) and cHDL (46%).

If we compare these resultados with the obtained in a transversal study made in the 17 autonomous communities of Spain, observe that the subjects studied attain more frequently the aims lipídicos recommended. In patients with DM2 and dislipidemia the approach global therapeutic has to consider, in addition to cLDL, the control of the levels of cHDL and of TG like secondary therapeutic aims, what can involve a change in our therapeutic attitude to achieve such aims. The main contribution of this work is the knowledge of the high prevalencia of dislipidemia (85,3%) in patients with DM2 of the Community of Castile-La Mancha and that the factors associated of independent form to the dislipidemia were the feminine sex and the antecedent of ECV. This knowledge is the first stair to implant the necessary means that make possible to improve the group of the profile lipídico, and, therefore, would have to be useful to establish strategies of continuous improvement that involve to all the agents involves (medical personnel, personnel of infirmary and sanitary authorities) in the implementation of the clinical guides and in improving the adherencia of the patients. Our results indicate that frequently it exists more than an alteration of the values plasmáticos of lipids. Like this, 23,7% showed conjoint alterations of cLDL and cHDL; 14,7%, of cLDL, cHDL and TG and, 6,6%, of the 4 parameters. On the other hand, the CT, cHDL and cLDL were significantly greater in women and the TG were significantly Mayanin in men; these findings are similar to the described in a study made in Catalonia. In the Or.K. Prospective Diabetes Study 27, observed that the CT, cHDL and the cLDL were significantly greater in women, what saves relation with the encontrado in our study.

By means of the analysis multivariable, identify that the feminine sex and the personal antecedent of ECV associate of independent way with the dislipidemia, above the age and of the HbA1c.

The prevalencia of dislipidemia sand associated with the feminine sex, what was consistent with other studies [4]. Regarding the association between sex and dislipidemia, in the current investigation the feminine sex was the most affected by dislipidemia, although 52,1% of the participants were of masculine sex. The association of both categorical variables by means of the analysis multivariante allowed to estimate that belong to the feminine sex in this group of patients increased in almost 3 times the relative risk to present dislipidemia. The perfil lipídico altered is a characteristic of the DM and confers greater risk to present ECV, especially EAC. The relative risk of coronary cardiac illness fatal associated with the DM is 50% higher in the women that in the men. The caused the greater risk of coronary cardiopathy in women with DM still does not know completely. However, the changes induced by the DM2 in some factors of cardiovascular risk, like the cLDL, cHDL, TG and the PA, have found more pronounced in the women that in the men, and this can explain the greater increase in the risk of arterioesclerosis in women diabéticas. Besides, the differences between the sexes in the profile lipídico could exert a paper in the most negative impact that has gave itabetes on the cardiovascular risk in the women in comparison with the men. Likewise, it has posited that the increase of the prevalencia of the dislipidemia in the women of age advanced can be related with the changes hormonales in the pre- and posmenopausia. The prevalencia of dislipidemia associated with the personal antecedent of ECV [6]. In the current investigation, the antecedent of ECV was significantly more prevalente in the masculine sex (39,5%) and almost 4 of each 10 of patients with dislipidemia had the antecedent of ECV (35,8%). The association of both categorical variables by means of the analysis multivariante allowed to estimate that have the personal antecedent of ECV in this group of patients increased in 3,5 times the risk to present sayslipidemia [7]. In this sense, is important to emphasize that the hipercolesterolemia is a factor of risk very prevalente in patients with ECV and confers special risk to suffer it, especially cardiopathy isquémica. Likewise, the high levels of CT and

cLDL are between the most important factors of risk of ECV, the cHDL low and the TG high are independent factors of risk of ECV and the treatment with estatinas has a beneficial effect in the incidence of the ECV aterosclerótica [8]. Our estudior presents diverse limitations and fortresses. Between the main limitations find the inherent to the type of study (longitudinal) and of analysis of the information; in this sense has to recognise the presence of the bias of survival, the impossibility to generalise the results to populations with different characteristics to the described; to his time, is necessary to make studies prospectivos that can confirm these results and analyse with greater precision the variables associated tol to prevalencia of dislipidemia.

Of the present study fits to stand out the sampling in which it is based, that is a representative sample of Castile-La Mancha, as well as the fact that it have been objetivado by several observers, what does it more damtativo in the recolección of data. Lto comparison of our results with the studies published to national and international level allows us see the consistency of the data. Besides, other variables could be predictores valid of dislipidemia. Our study did not take into account the possible modifications of the therapy hipolipidemiante and the therapeutic fulfillment of the patients. Finally, the longitudinal design is very used, since his cost is relativaminferior body to the of other designs epidemiológicos, like the transversal studies, and provide notable information and of fast form for the management of the services of health.

Because of the importance of the object of analysis that occupies us, believe necessary recalcar the importance to follow investigating in this line.

Conclusions

This investigation shows that in the patients with DM2 of Castile-La Mancha there is a high prevalencia of dislipidemia. The factors of risk associated of form independiente were the feminine sex and the personal antecedent of ECV. In sight of these results, exists the need of a handle integral and intensive of the dislipidemia, for which has to try improve the metabolic control of the diabetes, disminuir the obesity and promote changes in the lifestyles (cessation of the habit tabáquico, physical exercise and decrease of the consumption of saturated fats and of alcohol), with the end to diminish the ECV and to improve the quality of individual and collective life ofand sta population.

References

1. To CM, Alonso KR (2016) Dislipidemia diabética. *Rev Medical Clinical The Earls* 27: 152-159.
2. (2011) The silent illness. *Change* 16: 36-37.
3. Levey AS, Eckardt KU, Tsukamoto Y, Levin A, Coresh J, et al. (2005) Definition and classification of chronic kidney disease: To position statement from Kidney Disease: Improving Global Outcomes (KDIGO). *Kidney Int* 67: 2089-2100. [Crossref]
4. <http://www.revistaalad.com/pdfs/0702rev.pdf>
5. Pedro-Botet J, Benaiges D, Pedragosa À (2012) Dislipidemia diabética, macro and microangiopatía. *Clinica e Investigación en Arteriosclerosis* 24: 299-305.
6. Coast B, Neighbourhood F, Bolívar B, Castell C (2007) Primary prevention of the diabetes type 2 in Catalonia by means of the intervention on the lifestyle in people of high risk. *Med Clin (Brac)* 128: 699-704. [Crossref]
7. https://www.researchgate.net/publication/325079144_diabetes_mellitus_y_riesgo_cardiovascular_actualizacion_de_las_recomendaciones_del_grupo_de_trabajo_de_diabetes_y_riesgo_cardiovascular_de_la_sociedad_espanola_de_diabetes_sed_2018
8. <https://www.medigraphic.com/pdfs/facmed/un-2001/un011i.pdf>

Copyright: ©2020 Tébar DO. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.