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HYPERTRIGLYCERIDEMIC WAIST AND ARTERIAL HYPERTENSION IN ADULTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

CINTURA HIPERTRIGLICERIDÉMICA E HIPERTENSIÓN ARTERIAL EN ADULTOS: UNA REVISIÓN SISTEMÁTICA y METAANÁLISIS

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ABSTRACT

Objective: Develop a systematic review and meta-analysis to determine the association between hypertriglyceridemic waist (CHTG) and arterial hypertension (HBP) in adults. **Methods:** The present study is a systematic review (SR) with meta-analysis of analytical cross-sectional observational studies. Search strategies will be used in different databases, which will be Pubmed, SCOPUS, Web of Science, Embase. The qualitative analysis was presented in a table with the characteristics of each study. For quantitative analysis, random-effects meta-analysis was performed due to the heterogeneity of the studies. These variables were compared using Odds Ratios (OR) as a measure of association with their corresponding 95% confidence interval. **Results:** Five studies were included for statistical analysis. Overall, a statistically significant association was found between both variables (OR: 1.36; 95% CI 1.07 to 1.71). In turn, there was a high heterogeneity (I squared 92%). **Conclusions:** This SR found that CHTG is associated with the presence of hypertension. However, given the few studies found, it is recommended to carry out more primary studies with a prospective design before carrying out a next SR on the subject, and with standardized cut-off points to make a more homogeneous comparability.

Keywords: Hypertriglyceridemic waist; Hypertension; Adults; Systematic review. (Source: MESH-NLM)

RESUMEN

Objetivo: Desarrollar una revisión sistemática y metaanálisis para determinar la asociación entre la cintura hipertrigliceridémica (CHTG) e hipertensión arterial (HTA) en adultos. **Métodos:** El presente estudio es una revisión sistemática (RS) con metanálisis de estudios observacionales de corte transversal analítico. Se utilizarán estrategias de búsqueda en diferentes bases de datos las cuales serán Pubmed, SCOPUS, Web of Science, Embase. El análisis cualitativo fue presentado en una tabla con las características de cada estudio. Para el análisis cuantitativo, se realizó el metaanálisis de efectos aleatorios debido a la heterogeneidad de los estudios. Dichas variables fueron comparadas usando como medida de asociación Odds Ratios (OR) con su correspondiente intervalo de confianza al 95%. **Resultados:** Se incluyeron 5 estudios para el análisis estadístico. De manera global, se encontró asociación estadísticamente significativa entre ambas variables (OR: 1,36; IC 95% 1,07 a 1,71). A su vez, se presentó una alta heterogeneidad (I cuadrado del 92%). **Conclusiones:** La presente RS encontró que la CHTG está asociado con la presencia de HTA. No obstante, dado los pocos estudios encontrados, se recomienda la realización de más estudios primarios con un diseño prospectivo antes de la realización de una siguiente RS del tema, y con puntos de corte estandarizados para hacer una comparabilidad más homogénea.

Palabras clave: Cintura hipertrigliceridémica, hipertensión arterial, adultos, Revisión Sistemática. (Fuente: DeCS- BIREME)

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INTRODUCTION

Arterial hypertension (HTN) is one of the adults' most common chronic diseases. It is responsible for approximately 8.5 million deaths from strokes, ischemic heart disease, and other vascular and kidney diseases worldwide[1].

From 1990 to 2019, the number of people over 30 with high blood pressure doubled[2]. Globally, the prevalence of AHT fluctuates around 30% [3]. In Peru, the prevalence of AHT is estimated at 21.7%[4].

As it is a silent disease that can be detected from the first level of care, searching for ways to reach the diagnosis using easily accessible instruments is an essential task of the health system, as well as detecting the factors associated with its appearance. Of the numerous publications that have been made about AHT and its risk factors, there are currently works on its association with various metabolic alterations [5,6]; however, insufficient emphasis has been placed on its relationship with visceral fat.

It is known that the hypertriglyceridemic waist (CHTG) has been proposed in recent years as a tool for recognizing individuals with insulin resistance, prediabetes, and diabetes [7-10]. Likewise, this has been determined as a useful tool at the cardiovascular level [11,12] since it evaluates both serum triglyceride levels and pathological abdominal waist, two measurements that can be easily taken from the first level of care, which is related to levels of pathological conditions can result in an indicator of chronic non-communicable diseases such as high blood pressure [13-15].

Despite the presence of studies between AHT and CHTG, there has not been a complete analysis that evaluates whether this association exists and what its magnitude is. For this reason, a systematic review and meta-analysis were carried out in the present investigation to determine the association between CHTG and hypertension in adults.

METHODS

Design and study área

This study is a systematic review (SR) with a meta-analysis of analytical cross-sectional observational studies.

The PRISMA 2020 statement (Preferred Reporting Items for Systematic reviews and Meta-Analyses) was used as a guide(16). This SR was registered in PROSPERO (ID: CRD42022325900) (Available at: http://www.crd.york.ac.uk/prospero/)

Search strategy

Search strategies will be used in different databases, which will be Pubmed, SCOPUS, Web of Science, Embase. The key terms used were: Hypertension and Hypertriglyceridemic Waist. The search strategy for each database is available in Supplementary Annex 1.

Selection of studies

The selection criteria included CHTG and AHT, analytical observational studies (case-control studies, cohort studies, and cross-sectional analyses), and those carried out in the population over 18 years of age. Papers that were in a language other than English, Spanish, Portuguese or French that cannot be obtained in their full version, case reports, case series, ecological studies, letters to the editor, review articles, and secondary studies were excluded, and conference abstracts.

The Rayyan software was used to select the articles from the databases above. Two main researchers participated in the selection of studies, who independently reviewed the titles and abstracts of all the articles found to find those that met the selection criteria and eliminate duplicate articles. The software is available at: https://rayyan.qcri.org.

The researchers classified the studies and compared them with the observations given. If the two researchers agreed and had independently approved the study, it was selected. If both did not agree and had each independently excluded the study, it was not included. In case of conflict, if one of the two researchers wanted to include an article and the other did not, a third reviewer's intervention was requested to make the final decision.

After the initial selection, the evaluation of the full text of all the articles included by the researchers in the previous step continues. Additionally, the bibliographic references of those studies that cite them were searched to find studies that were not included in the initial search. Each reviewed article selected in the previous stages was included in a Sheet of the EXCEL 2022 program where it was finally placed if the study was included; if it was not included in the review, the reason for non-inclusion was written.

Data extraction and qualitative analysis

The Microsoft Excel 2022 program was used to collect the following data for each selected article: Author, year, country, study design, sample size, percentage of males, the mean or median age of the population, selection criteria, the prevalence of hypertriglyceridemic waist, the cut-off point used for abdominal waist, the prevalence of arterial hypertension, the measure of association, adjustment of variables.

Risk of bias

the risk of bias tool was used New Castle Ottawa for cohort studies[17] and the one modified in the review by Modesti et al. for cross-sectional studies[18].

Quantitative analysis

For the qualitative analysis, a table was presented with the characteristics of each study. For quantitative analysis, a random-effects meta-analysis was performed due to the heterogeneity of the studies. The variables of interest were worked in a dichotomous way, being the independent variable of the study, the CHTG, and the dependent variable, the AHT, expressed in whether there is the presence or absence of the variable in question. The dichotomous data presented were compared using Odds Ratios (OR) as a measure of association with their corresponding 95% confidence interval.

In the event that the study showed some other measure of association (for example, prevalence ratios), an email was sent to the corresponding author of the respective manuscript, to request if they could share said measure as OR.

Finally, the variability between studies was evaluated with the I squared (I2)[19], which was considered up to 40% as a cut-off point according to Cochrane, with <40% being a possibly insignificant heterogeneity and >40% heterogeneity representative moderate to high [20].

Ethical aspects

This study analyzes primary studies published in scientific journals for which no patient intervention exists. However, this was submitted for evaluation by the Ethics Committee of the Faculty of Human Medicine of Ricardo Palma University (Code: PG015-2022).

RESULTS

Eligible studies

A total of 149 published studies were identified. After removing the duplicate studies [55] recognized by the program and the investigators, 94 publications were evaluated through title and abstract. Then, if 67 articles were excluded because they did not meet the required criteria for the study evaluated through the title and abstract, there were 27 remaining studies, which were analyzed in full text, and 5 were excluded because they did not belong to the category of required studies or be only descriptive studies. The inclusion and exclusion criteria were applied within the final group of 22 studies, leaving 6 studies included [10,15,21-23]. Additional supplementary material will describe the final reasons for the 22 studies in the latter group.

Characteristics of the studies

Within 6 included studies (n=25814) with a sample made up of 354 to 9015 participants, 5 cross-sectional studies and 1 cohort study (of 7 years duration) were found, with respect to gender only 2 studies had a higher percentage of men in their population, the percentages of men in the population ranged from 23.7% to 51.8%. Regarding the age of the population, the cut-off point to be defined for the studies was 40 years (3 articles), 20 years (1 article), >18 years

(2 articles); the mean/median age of the population ranged from 40 to 65 years.

CTHG had a prevalence of 13.96% to 56.9%. Pathological waist circumference was defined by 3 studies with the cut-off point given by the NCEP-ATP III [34] ≥88cm for women and ≥102cm for men; 2 studies used the cut-off point according to IFD ≥ 80cm for women and ≥ 90 for men; only 1 study used two different parameters, both NCEP-ATP III and JIS ≥80cm for women and ≥94cm for men. Cut-off points for triglycerides ≥ 150 mg/dl. On the other hand, hypertension had a prevalence of 12.48% to 84.1%; the cut-off point was ≥ 140/90 mmHg.

Risk of bias assessment

Of the 6 studies, 5 were assessed using the modified NCO tool for cross-sectional studies and 1 was assessed using the NCO tool for cohort studies. Of all the studies, only 2 did not justify whether the sample size was satisfactory and 2 did not compare the characteristics of those surveyed and those not surveyed. Assessment of publication bias using the funnel plot was not performed due to the number of studies (<10) (20). Finally, 5 studies had a final score of 7 or 8 evaluated as low risk, and only 1 study had a score of 5 evaluated as a moderate risk study (Table 1 and 2).

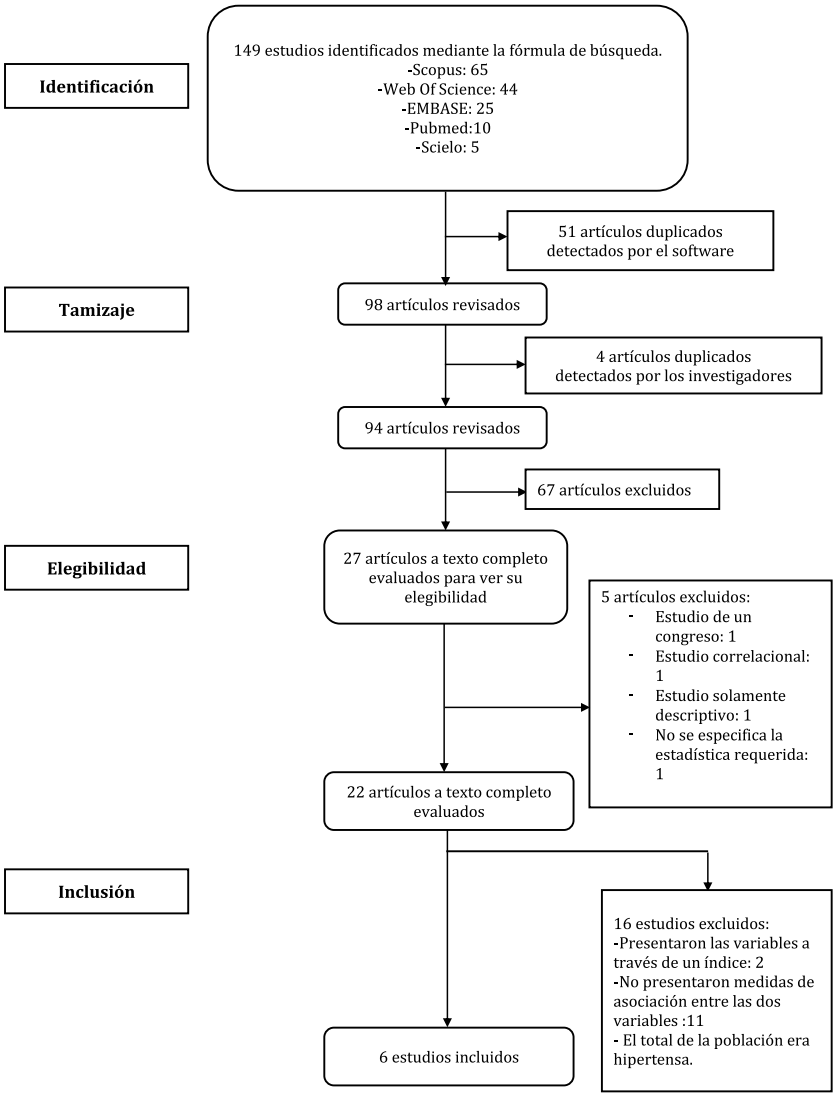

Figure 1. Flowchart.

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Table 1. Evaluation of the quality of the included studies using the Newcastle-Ottawa Scale (NOS) adapted for cross-sectional studies.

	Selection				Comparability		Result			
Author, years	Representativeness of the sample [1]	Sample size [2]	Determination of exposure [3]	Non-respondents [4]	Study controls for the most important factor [5]	Study controls for any additional factors [6]	Evaluation of the result [7]	Appropriate statistical analysis [8]	Score	Final Judgment
Yan Xuan MS et al, 2022	★	★	★	★		★★	★	★	8	Low Irrigation
Vera-Ponce VJ et al, 2022	★	★	★	★		★★		★	7	Low Irrigation
Tangvarasittichai S et al, 2015	★		★	★		★★	★	★	7	Low Irrigation
Fernández García JC et al, 2020	★	★	★			★★	★	★	7	Low Irrigation
Taloyan M et al, 2012	★		★★					★	5	Moderate Risk

[1] Representativeness of the sample: A star to studies with random sampling or census.
[2] Sample size: one star was assigned to studies with a justified and satisfactory sample size.
[3] Determination of exposure: The way in which the dependent variable has been measured is clearly explained
[4] Non-respondents: If the comparability between the characteristics of the respondents and non-respondents was established and the response rate was satisfactory, a star was assigned.
[5] The study controls for the most important factor: An adjustment has been made, either methodological or statistical, for the most important confounding variable
[6] The study controls for any additional factor: An adjustment has been made, either methodological or statistical, for other confounding variables
[7] Outcome assessment: If the study explicitly mentioned how self-medication was defined and how long the recovery period was, it was given one star.
[8] Adequate statistical analysis: One star was given if a complex sample was not used and the sample was calculated correctly, or if a complex sample was used and such a sample was considered to estimate the prevalence of self-medication.

Table 2. Evaluation of the quality of the included studies using the Newcastle-Ottawa Scale (NOS) adapted for cohort studies.

	Selection				Comparability		Result				
Author, years	Representativeness of the exposed cohort[1]	Selection of the unexposed cohort[2]	Verification of exposure[3]	Result of interest not present at the beginningng of the study[4]	Control of the study by the most important factor (sex/age)[5]	Study controls for any important additional factor[6]	Outcome assess-ment[7]	Sufficient duration of follow-up[8]	Adequate cohort follow-up	Score	Final Judg-ment
Janghorbani M et al, 2017	★	★	★	★		★	★	★	★	8	Low Irrigation

[1] Representativeness of exposed cohort: is truly representative or somewhat representative of the community.

[2] Selection of the unexposed cohort: Drawn from the same community as the exposed cohort.

[3] Comparison check: comes from secure registry as (surgical); or structured interview.

[4] Demonstration that the outcome of interest was not present at the start of the study: star if not present.

[5] Comparability of cohorts based on design or analysis: study controls existed for important factors; or for any additional study factors (controlling for important secondary factors).

[6] Evaluation of results: it is an independent blind evaluation or through a registration link.

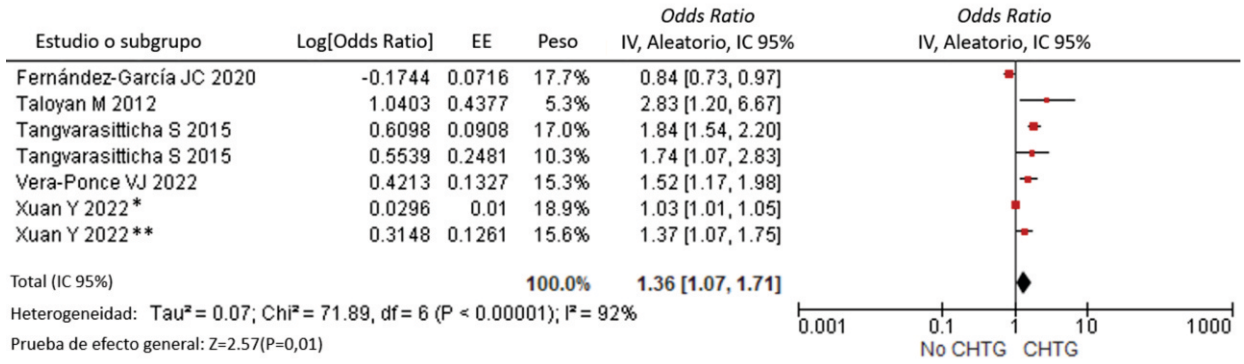
[7] Was the follow-up long enough for the results to occur? Star if it was long enough.

[8] Adequacy of cohort follow-up: whether follow-up is complete; or if subjects lost to follow-up are unlikely to introduce bias; or if there is a description provided of the missed traces.

Table 2. Characteristics and results of the included studies on the association between CHTG and HT.

Author	Year	Country	Study design	Sample size	Sex (% of men)	Mean/ Median age of the sample	Selection criteria	Prevalence of CHTG	Criteria for cut-of abdominal perimeter	Prevalence of AHT	Association measure	Adjustment of variables
YanXuan MS, et al.	2022	China	Cross	- sectional 9015	Men 3933 (43.62%)	60	**Inclusion**: Participants aged 40 years and over; minimum 5 years of residence in Shanghai, treated at the health center of the luwan-Ruijim branch. **Exclusion**: Participants who did not give or are unable to give their consent; pregnant; participants with critical illness such as: cancer, organ transplant or dialysis treatments; participants with missing data on blood pressure, triglyceride level, waist circumference; participants outside the selection period; participants who did not finish with the corresponding controls.	1909 (21.2%)	IDF	7426 (82.3%)	OR 1.28; 95% CI: (1.04,1.58) Men 1.03 (1.01,1.04) Women 1.37 (1.07,1.77)	Age, sex, BMI, smoking, alcohol consumption, physical activity, educational level, diabetes Mellitus.
Vera-Ponce VJ, et al.	2022	Peru	Transversal	4090	Men 2029 (49.6%)	40	**Inclusion**: ENINBSC participants aged 20 years and over **Exclusion**: Participants who changed their usual diet due to illness; that do not obtain the complete data of the variables of interest.	JIS (218.49%) ATPII (13.96%)	ATP III	509 (12.48%)	OR 1.52; 95% CI 1.17 to 1.98	Age, sex, BMI, smoking, alcohol consumption, physical activity, place of residence.
Janghorbani M , et al	2017	Iran	Cohort	1417	Initial sample 3483	42.6	**Inclusion**: First-degree relatives of patients with type 2 Diabetes	22.1% of those with CTHG	ATP III	Incidence 281 (19.8%)	OR 2.29 95% CI (1.55-3.38)	Age, sex, plasma glucose in fasting

					Men 919 (26.39%)		Mellitus (DM2). **Exclusion**: Participants with onset of DM2 or prevalent hypertension; who did not attend the follow-up exam; pregnant ; participants with missing data.	progressed to HT 14.6% of those without CHTG progressed to HT				
Tangvarasittichai S. , et al	2015	Thailand	Cross	sectional 4206	Men 997 (23.7%)	53	**Inclusion**: Participants aged 40 years and over; participants who are located within the 7 selected regions of Thailand. **Exclusion**: Participants with known end-stage renal failure, cancer, or any life-threatening disease; participants who present during the selection an infectious process.	Men 236 (23.7%) Women 1131 (35.2%)	IDF	Men (56.12%) Women (40.7%)	OR Men 1.74; 95% CI (1.07,2.84) Women 1.84; 95% CI (1.54, 2.21)	Age, sex, BMI, smoking, alcohol consumption, high triglyceride levels, low HDL levels and high cholesterol levels
Fernández García JC , et al	2020	Spain	Cross	sectional 6732	Men 3488 (51.8%)	65	**Inclusion**: Men participants in the age range 55-75 years and women in the age range 60-75 years with overweight or obesity (BMI ≥ 27 kg and < 40 kg/m2), and who present at least 3 criteria of the syndrome metabolic. **Exclusion**: Participants with a history of CVD or cancer in the last 5 years (with the exception of non-melanoma skin cancer); with inability to follow the recommended diet or inability to perform physical activity; with low probability of	2574 (38.2%)	ATP III	2100 (81.6%) with CHTG 3497 (84.1%) without CHTG	OR 0.84; 95% CI (0.73, 0.96)	Age, BMI, smoking, sedentary lifestyle, educational level, physical activity, adherence to the Mediterranean diet, presence of comorbidities (diabetes mellitus or arterial hypertension)
							changing eating habits; that they will not attend the scheduled visits for the intervention; who is bedridden or immobile, pregnant or hospitalized at the time of the study; participants who present a serious psychiatric disorder, addiction to alcohol consumption, drug addiction.					
Marina Taloyan, et al	2012	Sweden	Cross	354	Assyrian men /Syrians 173 (48.9) Swedes 181 (51.1%)	Assyrians/Syrian: 61 Swedes: 64	**Inclusion**: Participants with DM2 residing in Södertälje-Sweden who were selected from the 4 primary care centers. **Exclusion**: Participants who were not Assyrian/Syrian or Swedish; who did not complete their studies.	Assyrians /Syrians (55.2%) Swedes (56.9%)	ATP III	Assyrians/Syrians 100 (58%) Swedes 139 (77%)	OR 2.83; 95% CI (1.20, 6.71)	Age, sex, elevated total cholesterol levels, elevated triglyceride levels



*In the male group
**In the female group

Figure 2. Forest plot of random effects in obesity according to body mass index.

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Meta-analysis for CHTG and HT

Regarding the analysis of CHTG and HT, the studies that independently presented a statistically significant association were the study by Taloyan et al. [23] (OR: 2.83; CI 95% 1.20 to 6 .67), Tangvarasittichai et al. [22] (female group; OR 1.84; 95% CI 1.54 to 2.20) and Vera-Ponce et al. [15] (OR 1.52; 95% CI 1, 17 to 1.98) (Figure 2). Finally, a statistically significant association was found globally between both variables of interest (OR: 1.36; 95% CI 1.07 to 1.71).

All the studies that were part of the meta-analysis of cross-sectional studies presented a high heterogeneity Chi 2 p<0.001, I2 (92%). In addition, no meta-analysis of the cohort subgroup was performed because only one study was part of it, Janghorbani et al. [21] (OR: 2.29; 95% CI (1.55 to 3.38) p<0.001, being independently statistically significant.

DISCUSSION

This is the first SR combined with a meta-analysis that sought the association between TCHG and AHT in the adult population. A significant association was found between both variables of interest. However, it should be considered that there are still few studies on the subject, which is why we worked practically only with cross-sectional studies. Moreover, these works differed in several aspects, one of the main ones being the country of origin of the study. If we organize them into continents, we find the following classification: three studies of the Asian continent, two studies from the European continent, and only one from America.

Overall, a statistically significant association was found. This shows that despite the heterogeneity of the studies, the association with arterial hypertension was preserved. Independently, it has been seen in the study by Vera-Ponce VJ et al. [15] being the only included study that integrated two different measures of abdominal circumference, also achieving that its association with arterial hypertension in said population is maintained.

Within each study, the heterogeneity found may be due to different conditions; for example, Taloyan M et al [23] took people from Assyria/Syria and Sweden as the specific population; Fernández-García JC et al [10] took overweight or obese participants from specific age and BMI ranges; while Janghorbani M et al [21] only took first-degree relatives of patients with Diabetes Mellitus.

On the other hand, the cut-off points used as parameters in the abdominal waist should be mentioned. Although ATPIII BP values have been used as the classic and comparable cut-off between studies, several studies have considered using the most suitable for their own population, as recommended by the IDF or JIS criteria.

For this reason, it is necessary to clarify a standard definition of AP, to increase homogeneityespecially when research work is carried out [24].

The association between CHTG and hypertension can be seen from two angles: the presence of obesity and hypertriglyceridemia. First, choosing the abdominal waist as a marker of obesity, specifically of fatty adiposity, is important. Although BMI is often used to assess general obesity as a cardiovascular risk [25], many studies have considered WC a more specific marker [26-28]. In this way, the excessive release of fatty acids that exceeds the storage and oxidation capacity in tissues such as muscle, liver and pancreatic beta cell; therefore, there is the activation of other alternative metabolic pathways, which are harmful to the cell and lead to the generation of reactive oxygen species (ROS) and the accumulation of toxic intracellular metabolites. Activation of this systemic proinflammatory process also activates the sympathetic nervous system. This increases peripheral vascular resistance by stimulating the alpha receptors of the blood vessels. While at the level of the renal glomerulus, beta 1 receptors are stimulated, releasing plasmatic renin, and activating the renin-angiotensin-aldosterone system. This is how sodium and water retention occurs, increasing long-term cardiac output, in addition to the additional peripheral vasoconstrictor effect of angiotensin II [29,30].

Serum triglycerides, which are transported by lipoproteins, specifically very low-density lipoproteins. On the one hand, this biochemical parameter alone is a good translator of increased abdominal fat. While it is also known that hypertriglyceridemia is related to the atherogenic and proinflammatory process, causing long-term endothelial dysfunction, which is considered the substrate of arterial hypertension [31,32].

it is important to consider the following limitations. In the first place, it is a systematic review with meta-analysis only in analytical cross-sectional studies since the causality of the association found cannot be proven; however, it is the first global step of how the analytical behavior of both variables should be. Second, as described above, different guides and cut-off points have been used to measure waist circumference in studies around the world, which can be seen reflected in the diversity of selected studies; however, being the first systematic review that addresses these two variables of interest, it was decided to perform a meta-analysis and maintain the statistical value despite the high heterogeneity presented. Third, although it would have been ideal to working with prospective studies, only one was found that met the proposed criteria.

CONCLUSIONS

This SR found that CHTG is associated with the presence of AHT. However, given the few studies found, it is recommended to carry out more primary studies with a prospective design before carrying out the next SR on the subject and with standardized cut-off points to make more homogeneous comparability. Suppose these results are confirmed in subsequent studies. In that case, CHTG could be considered a predictive marker for long-term hypertension, with a fairly affordable utility in daily clinical practice, due to its low cost and easy application.

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