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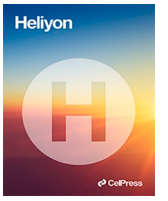

Research article

Association of GGT and hs-CRP with hypertension across different glycemic states in Saudi adults: A cross-sectional study

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ABSTRACT

Introduction: Atherosclerosis, hypertension, and diabetes (DM) is preceded by inflammation and endothelial dysfunction. Early detection of these risk factors is expected to improve prognosis. We aimed to examine the association between gamma-glutamyl transferase (GGT) and highly sensitive C-reactive protein (hs-CRP) with hypertension (HTN) in the presence and absence of dysglycaemia among Saudi adults not previously diagnosed with DM.

Methods: adults were recruited randomly from public healthcare centres in Jeddah. Demographic information, blood pressure, and anthropometric measurements were taken. Fasting blood samples were drawn to measure glucose, glycated haemoglobin, lipid profile, hs-CRP, and GGT. Blood was drawn again following a 1-h oral glucose tolerance test, and plasma glucose was measured.

Results: Mean GGT and hs-CRP were higher in people with HTN and dysglycaemia than those without both ($P < 0.001$). In people with HTN, those with intermediate hyperglycaemia (pre-DM) had significantly higher means of GGT and hs-CRP compared with those without ($P < 0.001$ and 0.013, respectively). In people with pre-DM, those with HTN had significantly higher means of GGT than those without ($P = 0.008$), but the increase in mean hs-CRP was not statistically significant. Mean GGT was higher in people with DM compared to means of those with pre-DM and HTN ($P = 0.04$).

Conclusion: An association between higher serum levels of hs-CRP and GGT and dysglycaemia exists, especially in hypertensive people. Monitoring both biomarkers in dysglycaemic people,

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especially if they have elevated blood pressure, is recommended to initiate therapeutic interventions.

1. Introduction

Atherosclerotic cardiovascular disease (CVDs), is the leading cause of death worldwide [1]. Atherosclerosis is associated with an inflammatory response of the vascular endothelium [2–4], resulting in the loss of its function and an imbalance in the production of essential vasodilator and vasoconstrictor molecules [3–6]. The risk of CVD increases with increasing blood pressure (BP) [7], making hypertension (HTN) the most important risk factor for CVD [8,9]. A strong association between dysglycaemia, and the risk of atherosclerotic CVD has been reported [9]. Moreover, it has been shown that several cardiometabolic risk factors, including HTN, dyslipidaemia, smoking, diabetes mellitus (DM), and obesity, can trigger and exacerbate endothelial dysfunction and are associated with inflammation in the vascular wall of resistance arteries [10,11].

Furthermore, HTN and DM often coexist, doubling the risk of CVD events in these patients [12]. In addition, it has also been reported that most people with intermediate hyperglycaemia suffer from essential HTN [13–15]. Women with elevated levels of the molecular biomarkers of endothelial dysfunction E-selectin, ICAM-1, and VCAM-1 were found to be at significantly increased risk of incident of type 2 diabetes millitus (T2DM), concluding that there is a role of endothelial dysfunction in the aetiology of T2DM [16]. Furthermore, a more recent study found that the coexistence of intermediate hyperglycaemia and HTN may increase endothelial dysfunction and inflammation [17]. Therefore, it is now well established that endothelial dysfunction and inflammation precede the development of atherosclerosis and some of its risk factors, namely HTN and DM. Thus, it could be deduced that the detection at an early stage of endothelial dysfunction and inflammation could help initiate preventive measures and improve the prognosis of the disease.

Most investigated endothelial dysfunction and inflammation biomarkers are not routinely measured in usual healthcare settings. However, the liver releases the acute-phase protein C-reactive protein (CRP) in response to interleukin-6 (IL-6) [18]. Indeed, increased levels of CRP have been reported to be associated with the increased risk of CVD [19–21]. In addition, lower levels of reduced glutathione (GSH) were reported in people with DM, indicating oxidative stress associated with chronic inflammation, and such low levels were associated with increased microvascular complications [22,23]. Measurement of GSH status is not practical in a clinical setting, and serum γ glutamyl transferase (GGT) has been suggested to be a surrogate biomarker of GSH [24–26]. In support of this suggestion, elevated levels of GGT have been reported to be associated with an increased risk of T2DM, HTN, and CVD events [26–28]. Indeed, the Multi-ethnic Study of Atherosclerosis (MESA) found significant associations between GGT, biomarkers of oxidative stress and endothelial dysfunction, so there were strong associations for increasing trends in those biomarkers [28]. Moreover, a study reported that serum GGT levels were significantly, and inversely, associated with endothelial dysfunction, an important early feature of the atherogenic process., and concluded that GGT might be an early marker of oxidative or other cellular stress that it is possibly directly related to the pathogenesis of endothelial dysfunction [29]. The role of GGT in endothelial dysfunction was further investigated in a study involving 500 Naïve hypertensive patients, reporting that the accuracy of GGT for identifying patients with endothelial dysfunction was 82.1 % so that serum GGT values may be considered a biomarker of early vascular damage [30].

CRP, highly sensitive CRP (hs-CRP), and GGT are routinely measured in most laboratories at healthcare centres. In an earlier study, we measured GGT and hs-CRP in people with T2DM but free from any DM complications. We found that high levels of both markers were associated with components of the metabolic syndrome and poor glycaemic control [31]. However, no studies have been carried out on non-diabetic Saudi adults to investigate this relationship. Therefore, this study aims to fill this gap by examining the association of the two routinely measured markers of early vascular damage and inflammation GGT and hs-CRP with HTN across different glycemic states in this population, focusing on intermediate hyperglycemia.

2. Materials and methods

2.1. Study design and sample collection

The data included in this study were acquired from a survey conducted between July 2016 and February 2017 in Jeddah city. The required data for a total of 1379 people were complete and included in the study. The Committee on the Ethics of Human Research approved the study at the Faculty of Medicine-King Abdulaziz University, Jeddah (Reference No. 1270–13), and participants obtained their consent form for the study. A full explanation of the study design and sampling methodology has been outlined earlier [32]. The sampling methodology summarises that adults were recruited from Primary Health Care (PHC) centre attendees in Jeddah, Saudi Arabia, between July 2016 and February 2017. People $\geq$18 years of age and not previously diagnosed with DM were included. Anyone reporting being previously diagnosed with DM, cancer, renal or liver disease, CVD, gastrointestinal diseases needing special diet, physical or mental disabilities, and pregnant women were excluded. Following signing an informed consent form, demographic, dietary, and lifestyle variables, as well as medical history and family history of chronic diseases, were gathered from recruits using a predesigned questionnaire. A fasting blood sample was taken for determination of fasting plasma glucose (FPG), glycated haemoglobin (HbA1c), lipid profile, hs-CRP, and GGT, followed by a 1-h oral glucose tolerance test (OGTT) [33,34], to screen for DM and intermediate hyperglycaemia. Anthropometric measurements [weight, height, waist circumference (WC)], and blood pressure (BP) were measured using standardised equipment and techniques. Weight and height were used to calculate the body mass index (BMI).

Hypertension was defined as SBP ≥140 and/or DBP ≥90 mm Hg or taking antihypertensive drug treatment [35].

2.2. Definitions of diabetes and intermediate hyperglycaemia (previously pre-DM)

Diabetes (DM) was defined as either HbA1c ≥ 6.5 %, FPG ≥7 mmol/L or 1 h-OGTT ≥11.1 mmol/L [36,37]. People with either HbA1c 5.7–6.4 % (39–46 mmol/mol), FPG 6.1–6.9 mmol/L (impaired fasting glucose; IFG)) or 1-h plasma glucose (1-hPG) 8.6–11.0 mmol/L (impaired glucose tolerance; IGT)) were considered to have intermediate hyperglycaemia (Pre-DM) [33].

2.3. Biochemical assays

Whole blood, serum, and plasma samples were sent regularly to an accredited laboratory by the College of American Pathologists at the National Guard Hospital in Jeddah. Plasma glucose and serum hs-CRP, GGT, total cholesterol (TC), high-density lipoprotein-cholesterol (HDL-C), and triglycerides (TG) levels were measured by spectrophotometric methods using Architect c8000 auto-analyzer (ABBOTT- USA). Low-density lipoprotein-cholesterol (LDL-C) was calculated using the Friedewald equation [38]. HbA1c was measured with high-pressure liquid chromatography (HPLC) using an automated HbA1c analyzer G8 (TOSOH Corporation-Japan).

Levels of GGT >86 for men and >30 U/L for women were considered high [39]. A level >3 mg/L of hs-CRP was considered to be associated with a high risk of CVD [40,41].

2.4. Statistical analysis

The data obtained were analysed using SPSS version 26. One-way ANOVA was used to compare the means of the five groups that were categorised based on the presence or absence of hypertension, dysglycaemia (DM and intermediate hyperglycaemia or pre-DM), and when normality was not confirmed by using the Kolmogorov-Smirnov test, the Kruskal-Wallis test was used. The Chi-square test was used to compare the distribution of categorical variables between the five groups. The association between clinical and biochemical variables and endothelial dysfunction and inflammation biomarkers was tested using Spearman's correlation. Logistic regression adjusted for age and gender was used to investigate the contribution of the presence of HTN and/or intermediate hyperglycaemia or DM to high hs-CRP and GGT. A p-value <0.05 (two-sided test) was accepted as statistically significant.

3. Results

A total of 1379 people were included in the study. The demographic, clinical and metabolic characteristics of the groups categorised based on the presence or absence of HTN, dysglycaemia, and intermediate hyperglycaemia (pre-DM) or DM are shown in Table 1; 799 people (57.9 %) had no HTN or dysglycaemia, 265 (19.2 %) had HTN only, 164 (11.9 %) had intermediate hyperglycaemia (pre-DM) only, 88 (6.4 %) had intermediate hyperglycaemia (pre-DM) and HTN and 63 (4.6 %) had DM. People with HTN and/or pre-DM or DM had higher means of age, BMI, SBP, DBP, FPG, 1hr-Glu, HbA1c, TC, TG, and LDL-c, and lower means of HDL-c (p

Table 1
Demographic and clinical characteristics of people with and without dysglycaemia and HTN.

	- Dysg, - HTN (n = 799)	- Dysg, + HTN (n = 265)	+ Pre-DM, - HTN (n = 164)	+ Pre-DM, + HTN (n = 88)	+ DM (n = 63)	P-value
Age (yrs)	29.2 (0.32)[a]	32.76 (0.71)[b]	36.84 (0.93)[c]	42.42 (1.5)[d]	41.84 (1.54)[d]	<0.001
Sex, n,%						
Male	410 (52.6 %)	182 (23.3 %)	89 (11.4 %)	53 (6.8 %)	46 (5.9 %)	<0.001
Female	389 (64.9 %)	83 (13.9 %)	75 (12.5 %)	35 (5.8 %)	17 (2.8 %)	
Smoking, n,%						
Smoker	163 (54.3 %)	62 (20.7 %)	30 (10 %)	26 (8.7 %)	19 (6.3 %)	0.085
Nonsmoker	636 (58.9 %)	203 (18.8 %)	134 (12.4 %)	62 (5.7 %)	44 (4.1 %)	
BMI	26.0 (0.19)[a]	29.3 (0.41)[b]	28.8 (0.45)[b]	31.7 (0.63)[c]	31.8 (0.81)[c]	<0.001
SBP	112 (0.35)[a]	131 (0.86)[b,c]	113 (0.71)[a]	134 (1.45)[c]	128 (3.24)[b]	<0.001
DBP	69 (0.32)[a]	84 (0.67)[c]	70 (0.67)[a]	85 (1.17)[c]	80 (1.57)[b]	<0.001
FPG (mmol/L)	4.18 (0.02)[a]	4.23 (0.04)[a]	4.64 (0.06)[b]	4.93 (0.09)[b]	7.06 (0.42)[c]	<0.001
1-hPG (mmol/L)	5.94 (0.05)[a]	6.04 (0.09)[a]	8.2 (0.15)[b]	8.49 (0.19)[b]	12.43 (0.59)[c]	<0.001
Hb A1c%	5.14 (0.01)[a]	5.15 (0.02)[a]	5.58 (0.03)[b]	5.56 (0.05)[b]	6.8 (0.2)[c]	<0.001
TC (mmol/L)	4.7 (0.03)[a]	4.87 (0.05)[a,b]	4.98 (0.08)[b,c]	5.22 (0.1)[c]	5.24 (0.11)[c]	<0.001
HDL-c (mmol/L)	1.38 (0.01)[a]	1.32 (0.02)[b]	1.34 (0.02)[a,b]	1.27 (0.03)[b]	1.26 (0.04)[b]	<0.001
TG (mmol/L)	1.12 (0.03)[a]	1.36 (0.05)[b]	1.3 (0.06)[a,b]	1.74 (0.1)[c]	2.09 (0.17)[c]	<0.001
LDL-c (mmol/L)	3.11 (0.03)[a]	3.28 (0.05)[b]	3.35 (0.07)[b,c]	3.58 (0.09)[c,d]	3.53 (0.11)[b,c]	<0.001

Dysglycemia (pre-DM and DM), FPG, fasting plasma glucose; 1-hPG, 1-h plasma glucose; TC, serum total cholesterol; HDL- C, serum high-density lipoprotein cholesterol; LDL, serum low-density lipoprotein cholesterol; TG, serum triglycerides; hs-CRP, serum highly sensitive C-reactive protein; GGT, gamma-glutamyl transferaseData are mean (SE) for continuous variables and n (%) for categorical variables. a, b, c, and d statistically significant differences between groups using one-way ANOVA ($p < 0.05$).

< 0.01) at least in the ANOVA overall between groups tests. Men were more likely to have HTN and/or DM than women ($P < 0.001$). A trend but no significant difference was observed for a higher presence of HTN and pre-DM or in smokers ($P = 0.085$).

3.1. Serum levels of hs-CRP and GGT by the presence or absence of hypertension, intermediate hyperglycaemia, and diabetes

Serum GGT and hs-CRP by the presence or absence of HTN, dysglycaemia, and intermediate hyperglycaemia (pre-DM) or DM are shown in Fig. 1. Mean serum GGT was 24.1 u/L in people with no HTN or dysglycaemia, 29.3 u/L in those with HTN only, 32.2 u/L in those with intermediate hyperglycaemia only, 40.4 u/L in those with intermediate hyperglycaemia and HTN, and 45.6 u/L in those with DM. Mean serum GGT was significantly higher in people with HTN and intermediate hyperglycaemia or DM compared with those who did not have HTN or dysglycaemia ($P < 0.001$ at least; Fig. 1). In people with HTN, those with intermediate hyperglycaemia had significantly higher mean GGT than those without intermediate hyperglycaemia ($P < 0.001$; Fig. 1). In people with intermediate hyperglycaemia, those with HTN had significantly higher mean GGT than those without HTN ($P = 0.008$; Fig. 1). Mean serum GGT was significantly higher in people with DM than those with intermediate hyperglycaemia and HTN ($P = 0.04$; Fig. 1).

Mean serum hs-CRP was 2.8 mg/L in people with no HTN or dysglycaemia, 3.6 mg/L in people with HTN only, 4.2 mg/L in people with intermediate hyperglycaemia only, 4.8 mg/L in people with intermediate hyperglycaemia and HTN, and 5.3 mg/L in people with DM. Mean serum hs-CRP was significantly higher in people with HTN and intermediate hyperglycaemia compared with those who did not have HTN and/or dysglycaemia ($P = 0.001$ at least; Fig. 1). In people with HTN, those with intermediate hyperglycaemia had significantly higher mean hs-CRP than those without intermediate hyperglycaemia ($P = 0.013$; Fig. 1). In people with intermediate hyperglycaemia, those with HTN had higher mean hs-CRP than those without HTN, but this did not reach statistical significance (Fig. 1). Mean serum hs-CRP was significantly higher in people with DM than those with intermediate hyperglycaemia and no HTN ($P = 0.024$; Fig. 1) but not with intermediate hyperglycaemia and HTN.

3.2. Correlations of demographic, biochemical and clinical data with GGT and hs-CRP

Age, BMI, SBP, DBP, FPG, Glu-1hr, HbA1c, TC, HDL-c, TG, and LDL-C correlated significantly with GGT and hs-CRP (all $p < 0.001$; Table 2). The Spearman's correlation with GGT but not with hs-CRP for elevated SBP and DBP were higher than those of glycemia (FPG, 1-hPG and HbA1c) (Table 2).

Logistic regression analysis with adjustment for age and sex was carried out (Table 3). The presence of dysglycaemia (intermediate hyperglycaemia and DM) significantly increased the odds of high GGT in both cases, regardless of the presence of HTN. Hypertension and/or dysglycaemia significantly increased the odds of high hs-CRP.

4. Discussion

Studies have established that the development of atherosclerosis and two important risk factors, namely hypertension and DM, is preceded by inflammation and endothelial dysfunction [4,17]. Therefore, it is logical to suggest that detection of both at an early stage will aid in improving prognosis by initiating preventive measures.

The gender difference was found in the prevalence of HTN and/or DM, with men being more likely to be affected. Our study

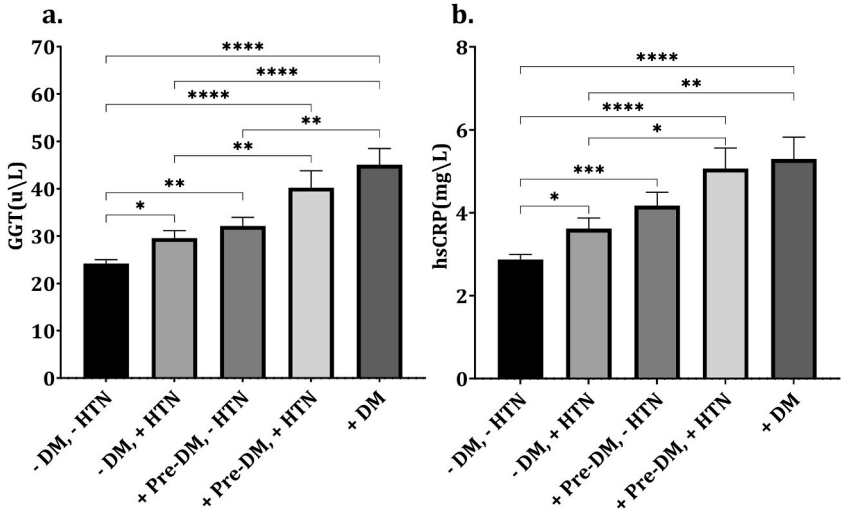

Fig. 1. Serum levels of GGT (U/L) and hs-CRP (mg/L) by the presence or absence of HTN, Pre-DM (intermediate hyperglycaemia), and DM. Data presented as mean +\- SD. Statistically significant differences between groups using the Kruskal-Wallis test ($p<0.005$). * $p<0.5$, ** $p<0.1$, *** $p<0.001$, **** $p<0.0001$. Pre-DM (intermediate hyperglycaemia).

Table 2
Correlations of demographic, biochemical and clinical data and GGT and hs-CRP.

	GGT		hs-CRP	
	Spearman's correlation	P-value	Spearman's correlation	P-value
Age	0.22	<0.001	0.261	<0.001
BMI	0.321	<0.001	0.525	<0.001
SBP	0.349	<0.001	0.13	<0.001
DBP	0.262	<0.001	0.128	<0.001
FPG	0.182	<0.001	0.16	<0.001
1-hPGl	0.25	<0.001	0.152	<0.001
HbA1c	0.201	<0.001	0.25	<0.001
TC	0.244	<0.001	0.111	<0.001
HDL-c	−0.318	<0.001	−0.178	<0.001
TG	0.44	<0.001	0.227	<0.001
LDL-c	0.264	<0.001	0.129	<0.001

Table 3
Odds ratios (OR) and 95 % confidence intervals (95 % CI) of glycemia status and HTN for high GGT and hs-CRP adjusted for age and sex.

	High GGT (>86 for men, and >30 U/L for women)		High hs-CRP (>3 mg/L)	
	OR (95 % CI)	P-value	OR (95 % CI)	P-value
No dysglycaemia* and no hypertension	reference		reference	
- Dysg, + hypertension	0.904 (0.434, 1.881)	0.786	1.438 (1.056, 1.958)	0.021
+ Pre-DM, - hypertension	2.695 (1.472, 4.931)	0.001	1.821 (1.262, 2.627)	0.001
+ Pre-DM, + hypertension	2.829 (1.318, 6.073)	0.008	1.93 (1.19, 3.129)	0.008
Diabetes	4.459 (1.995, 9.967)	<0.001	3.567 (2.003, 6.353)	<0.001

Dysglycemia denotes the presence of either intermediate hyperglycaemia (Pre-DM) or DM.

demonstrated a significant association between elevated serum gamma-glutamyl transferase (GGT) and high-sensitivity C-reactive protein (hs-CRP) levels with dysglycaemia and hypertension (HTN) in Saudi adults without prior diabetes diagnoses. GGT and hs-CRP levels were higher in individuals with HTN and dysglycaemia compared to those without these conditions, with intermediate hyperglycaemia (pre-DM) further amplifying these associations. Logistic regression analysis revealed that intermediate hyperglycaemia and diabetes mellitus (DM) significantly increased the odds of elevated GGT, independent of HTN, while HTN, pre-DM, and DM collectively increased the odds of elevated hs-CRP. Our results are in line with previous studies demonstrating a strong link between oxidative stress, inflammation, and glycaemic control [42,43] Additionally, we found that metabolic parameters such as BMI, lipid profile, and fasting glucose correlated strongly with both GGT and hs-CRP levels. Similar findings have been reported, including the association of the elevation of these two markers with metabolic abnormalities, hypertension, and cardiovascular risk [44].

In a previous study, HTN has been reported to increase the risk of macrovascular or microvascular complications in patients with T2DM [12]. The increased hs-CRP, a measure of inflammation, in our study of all people with dysglycaemia could explain the increased risk.

Our results agree with a Chinese study, which reported that the presence of prediabetes or HTN was associated with increased levels of serum markers of inflammation and endothelial dysfunction and that the coexistence of both together increased the levels further [17]. In the aforementioned Chinese study, different serum biomarkers were estimated, namely, (ICAM-1), (TNF-α), P-selectin, and interleukin-6 (IL-6). These biomarkers are difficult to measure in a clinical setting, unlike our measured markers, which are routinely available and could help in risk stratification and initiating management strategies to improve prognosis.

In line with our findings, elevated levels of CRP as a predictor of dysglycaemia were reported earlier in a large cohort study which was conducted in Korea between 2005 and 2011 on 22,946 men and women from 11 rural communities at baseline [42] to assess the associations of CRP with incident T2DM and to determine the joint effect of obesity and HTN on them. This study concluded that increased serum levels of CRP and its combination with obesity and HTN were associated with an increased risk of T2DM, an important and strong risk factor for atherosclerosis. Indeed, a direct link between early elevated hs-CRP and CVD incidence has been proven in another more recently published Korean study that suggested that regular hs-CRP testing is required to monitor its trends, thus helping in the development of treatment plans to prevent CVD [44], which substantiates our findings for the use of hs- CRP as a risk predictor for atherosclerosis further. Similar findings were reported in a review and meta-analysis, which covered 60 studies and evaluated the association between CRP level and risk of cardiovascular events, concluding that the risk of CVD increased with increasing serum CRP level [45].

Similar to our findings in this study, evidence from an observational study reported a significant association between increased GGT levels and prediabetes [46] and risk of T2DM. In another study, the relationship between the level of serum GGT and glucose intolerance in first-degree relatives (FDR) of T2DM patients was investigated, reporting increased glucose intolerance in those FDR, and suggested that measurement of serum GGT might help in predicting their future risk of DM [46]. In addition, high rates of elevated GGT levels among diabetic patients have been reported in many epidemiological studies over the last decades [47].

The association between elevated levels of GGT and HTN has received much attention. A Turkish study conducted on young

patients with prehypertension reported that these patients showed higher serum GGT levels than healthy subjects [48], which aligns with our findings in this study. In addition, like our findings, a large Korean study on apparently healthy subjects reported that the level of GGT was highly and positively correlated with both systolic and diastolic blood pressure [49]. The same study also reported a positive linear correlation between GGT levels with BMI, WC, FPG, TC, LDL-C, and TG levels, which is in line with our results.

However, results from various cross-sectional and longitudinal studies investigating the association of GGT level with the risk of HTN reported inconsistent, even opposite conclusions [50]. For example, in a cohort Chinese study that included hypertensive and normotensive subjects, plasma GGT was an independent predictor of new-onset HTN [51]. Moreover, a Korean study reported that Elevated serum GGT levels, even within the normal range, were found to be associated with a higher risk of incident HTN, particularly in drinkers and non-overweight individuals [52], emphasising the need for adjustment for various factors which have been shown to affect GGT levels, such as waist circumference and body mass index [52], HTN [51], DM [53], hyperuricemia [54] and genetic factors [55,56]. Nevertheless, an association between elevated serum GGT levels and the risk of CVDs, DM, and metabolic syndrome has been elucidated in various studies and meta-analysis [57–59], and level of serum GGT have been indicated to be an independent predictor of HTN, metabolic syndrome, DM, and coronary artery disease (CAD) [60], which supports our findings.

The association does not imply causation, and the causal role of elevated GGT on T2DM and HTN was investigated in various studies. A large Swiss study employing the Mendelian randomisation (MR) approach and using the rs2017869 variant of the GGT1 gene as an instrument to assess the causal relation of GGT with blood pressure and serum insulin levels reported that there was a direct causal relation of GGT with fasting insulin but not with BP [42]. A later and more detailed (MR) study in the Netherlands investigated the causal effect of GGT on DM and prediabetes using a genetic risk score based on a genome-wide association study (GWAS), concluding that the increased level of GGT was not the cause for prediabetes or T2DM and that a response to the disease might cause the reported association with dysglycaemia (reverse causation) or confounding factors [61].

Based on these findings and suggestions, the elevation in GGT noted in our study is likely due to increased oxidative stress, which is reported to lead to β-cell dysfunction and reduction in insulin action, thus resulting in increased insulin resistance [25,29]. Moreover, the noted elevation could reflect endothelial dysfunction [29,30], an early event in the atherogenic process. Therefore, it could be suggested that the elevation in serum GGT activity precedes the development of dysglycaemia and could reflect several different processes relevant to diabetes pathogenesis.

Based on the above, in order to institute preventive management plans to prevent or slow down the development of atherosclerosis, it might be prudent to monitor both hs-CRP and GGT levels in people at high risk of dysglycaemia, such as those who are overweight or obese and first-degree relatives of type 2 diabetic patients, especially if they have elevated blood pressure as well.

Our study has limitations as well as points of strength. The first limitation is its design, which is common in all cross-sectional studies, making an association between studied variables, but not causation, possible to suggest. Another limitation is that the number of included people with T2DM or pre-DM and HTN was relatively small compared to the other groups due to the inclusion criteria.

However, our study has many points of strength. First of all, it is the first study to be carried out on Saudi people not previously diagnosed with DM, thus excluding the effect of DM medications on measured biochemical variables. Secondly, PHCCs and participants were selected randomly to avoid bias in sample collection. Moreover, data collectors were all well-trained, and well-standardized methods were used to ensure data integrity. Finally, all biochemical measurements were carried out in one accredited laboratory to ensure the accuracy of the results.

5. Conclusions

In conclusion, our results highlight the association between higher serum hs- CRP and GGT levels and dysglycaemia in Saudi adults, especially in those with HTN. Monitoring both markers in people at high risk of dysglycaemia, such as those who are overweight or obese, and first-degree relatives of T2DM patients is recommended, especially if they had elevated blood pressure as well in order to initiate therapeutic interventions for preventing or slowing down the atherosclerotic process.

CRediT authorship contribution statement

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Informed consent statement

Informed consent was obtained from all subjects involved in the study.

Disclosure

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Declaration of generative AI and AI-assisted technologies in the writing process

No Generative AI was used during the preparation of this manuscript.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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