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ORIGINAL RESEARCH ARTICLE

# Clinical and Demographic Characteristics of Patients with Coexistent Hypertension, Type 2 Diabetes Mellitus, and Dyslipidemia: A Retrospective Study from India

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## Abstract

**Background** Coexisting hypertension, type 2 diabetes mellitus (T2DM), and dyslipidemia (triple disease) can lead to greater risk of cardiovascular morbidity and mortality. The present study sought to comprehend the prevalence, demographic traits, clinical traits, and treatment patterns in Indian patients with these coexisting conditions.

**Methods** An electronic medical record (EMR)-based, retrospective, multicenter, cross-sectional study was conducted, and data were collected for patients who were diagnosed with coexistent hypertension, T2DM, and dyslipidemia. Baseline patient variables evaluated were the percentage of patients with triple comorbidity, demographic characteristics, diagnostic laboratory parameters, and treatment pattern details.

**Results** Data from 4793 centers (clinics) were included, with a total of 6,722,173 patients. Of these, 427,835 (6.36%) patients were found to have coexistent hypertension, T2DM, and dyslipidemia. Most of the patients belonged to the 40–64 year age group (62.10%) and were males (57.00%), while 27.40% patients had a body mass index (BMI) within normal limits, 43.30% patients were pre-obese, and 20.90% patients were class 1 obese. Further, 3402 patients (0.80%) had a recorded history of smoking. Mean glycated hemoglobin (HbA1c) for the patients included in the study was 8.35 ± 1.96 g%. Mean systolic blood pressure (SBP) was 138.81 ± 19.59 mm Hg, while mean diastolic blood pressure (DBP) was 82.17 ± 10.35 mm Hg; 27.60% cases had SBP < 130 mm Hg, while 28.37% cases had DBP < 80 mm Hg. The mean low-density lipoprotein (LDL), total cholesterol, and high-density lipoprotein (HDL) in mg/dl were 98.38 ± 40.39, 174.75 ± 46.73, and 44.5 ± 10.05, respectively. Of the enrolled cases, 55.64% had serum LDL below 100 mg/dl, 72.03% cases had serum cholesterol below 200 mg/dl, and 44.15% males and 71.77% females had serum HDL below the normal prescribed range. The most common monotherapy used for managing hypertension was angiotensin receptor blockers (ARB) (24.80%), followed by beta-blockers (24.30%). The most common combinations administered for management of hypertension were antihypertensives with diuretics (14.30%), followed by ARB plus calcium channel blockers (CCB) (13.30%). For dyslipidemia, the majority of patients (56.60%) received lipid-lowering medication in combination with drugs for other comorbidities. The most common antidiabetic agents prescribed were biguanides (74.60%).

**Conclusions** Coexistence of triple disease is not uncommon in the Indian population, with middle-aged patients diagnosed as pre-obese and obese being affected more commonly and receiving treatment for the same. The present study highlights that, though there are medications against the three chronic conditions, the rate of uncontrolled cases of hypertension, T2DM, and dyslipidemia remains high. Coexistence of triple disease increases the risk of cardiovascular and renal complications, which need to be closely monitored and effectively treated.

## 1 Introduction

An imbalance in insulin production and action leads to hyperglycemia, which is an indicator of diabetes mellitus (T2DM) [1, 2]. According to the International Diabetes Federation, 537 million people (aged 20–79 years) globally had T2DM in 2021. By 2030, this figure is expected to reach 643 million, and by 2045, it will reach 783 million [3]. Ninety percent of all cases of diabetes are T2DM [3]. Another illness that significantly affects India's healthcare systems and cardiovascular health status is hypertension. More than half of all stroke fatalities and roughly a quarter of all deaths from coronary heart disease (CHD) in India

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**Key Points**

Middle-aged patients diagnosed as pre-obese and obese are more affected with hypertension, T2DM, and dyslipidemia.

The majority of patients with the triple comorbidity had uncontrolled T2DM, hypertension, and a deranged lipid profile despite being on treatment.

are directly attributable to hypertension [4]. Indian research estimated that 25% of rural and 33% of urban Indians had hypertension, with 42% of city dwellers and 25% of rural residents affected. Only 25% of Indians in rural areas and 38% in urban areas are receiving treatment for hypertension while only one-tenth of the hypertensive population in rural and urban India has their blood pressure (BP) under control [5]. A set of abnormalities of lipoprotein metabolism known as dyslipidemia includes excess or insufficient production of lipoproteins. Raised triglycerides, elevated low-density lipoprotein (LDL) cholesterol, and/or low high-density lipoproteins (HDL), often known as the protective cholesterol, are all possible components of dyslipidemia. It is a pathological disease when the levels of lipids are outside the prescribed range, and it can significantly increase cardiovascular morbidity and death. According to the National Health Portal of India, approximately 25–30% of urban and 15–20% of rural individuals in India have dyslipidemia. Although it affects both sexes, men are more likely to experience it. Individuals older than 60 years have a greater chance of developing dyslipidemia compared with the younger population [6]. In T2DM patients, several metabolic syndromes (MetS), such as dyslipidemia, hyperglycemia, and hypertension, serve as conduits for aggravating cardiovascular disease (CVD) risk factors [7, 8]. Various risk factors such as genetic predisposition, insulin resistance, dyslipidemia, and obesity play an intricate role in occurrence of both T2DM and hypertension. Several processes, including increased production of advanced glycation end products (AGEs) and activation of the AGE receptor for advanced glycation end products (RAGE axis), oxidative stress, and inflammation, are involved in the development of vascular complications of diabetes as a result of chronic hyperglycemia and insulin resistance [9]. Since hypertension itself is characterized by vascular dysfunction and damage, it is a significant risk factor for diabetes-related vascular problems. Hence, T2DM, hypertension, and obesity closely interplay in increasing the risk of cardiovascular diseases [10].

Studies evaluating the demographic information and clinical traits of individuals with each of these comorbidities independently have been published, but the coexistence of these disorders in the Indian population has not been investigated. Therefore, the purpose of this study was to evaluate the prevalence of coexisting hypertension, T2DM, and dyslipidemia (triple disease) in the Indian population. Additionally, this study sought to comprehend the demographic traits, clinical traits, and practice patterns (treatment patterns) of Indian patients who had coexisting triple disease.

## 2 Methods

### 2.1 Study Design

An electronic medical records (EMR)-based, retrospective, multicenter, cross-sectional, database study was conducted, and the data were collected for patients who were diagnosed with coexistent hypertension, T2DM, and dyslipidemia. An informed consent waiver was obtained from the ethics committee, as this was a nonexperimental, retrospective data analysis study. Healthplix (https://healthplix.com/) operates from physician clinics across India. This EMR is used by the physicians to write prescriptions. These data (based on the agreement between doctors and Healthplix) were used for this EMR-based retrospective study. EMR records for the patients meeting the eligibility criteria from January 2021 to December 2021 were extracted and analyzed. Since the present study was an observational and database study, no additional tests or interventions were suggested.

Inclusion criteria: Adult patients of ≥18 years of age, mentioned on the EMR platform (other than the first visit on platform) with coexistent hypertension, type 2 diabetes mellitus, and dyslipidemia were included in the study.

Exclusion criteria: Patients with type 1 diabetes mellitus, familial hypercholesterolemia, pregnant women, and patients whose relevant data required in study as part of outcome measure was absent from the EMR database due to any reason were not a part of the study

Baseline patient variables evaluated were prevalence (this EMR is based in outpatient settings, for calculating prevalence, all the patients whose data were entered on to the EMR were taken as the base population) of the triple comorbidity, demographic characteristics (gender and age), BMI, and comorbidities. In addition, the baseline diagnostic laboratory parameters as well as the treatment pattern details were also noted. Baseline visit is the one when patients were diagnosed with (type 2 diabetes, hypertension, and dyslipidemia) for the first time on the EMR platform (other than the first visit on the platform). Data management was done in accordance with applicable regulatory requirements so that the integrity of the data can be ensured, e.g., removing errors and inconsistencies in the data. The data from the EMR were collected using data collection forms.

The American Diabetes Association (ADA) guidelines suggest a target HbA1c of < 7% for the patients on T2DM treatment. [11]. The diagnosis of normal or abnormal BP in the included patients was based on the American College of Cardiology/American Heart Association (ACC/AHA) guidelines, which mention that for hypertensive patients, the target for systolic BP (SBP) is < 130 mm Hg and/or their diastolic BP (DBP) is < 80 mm Hg following repeated examination [12]. Based on ATP-III classification, the considered targets for serum LDL, serum HDL, and total cholesterol are < 100 mg/dl, > 40 mg/dl, and < 200 mg/dl, respectively [13].

### 2.2 Statistical Analysis

All the included patients constituted the analysis population and all the available data obtained from the EMR were used for summary/analysis purposes. The included population was defined as patients who met the eligibility criteria. The data were analyzed using descriptive statistics. Quantitative data are presented as mean and median with standard deviation (SD) and range, respectively. Categorical data (e.g., gender, etc.) are presented by frequency and proportion. Clinical characteristics and practice patterns (treatment patterns) in patients with coexistent triple disease are presented descriptively.

## 3 Results

### 3.1 Patient Flow and Prevalence Data

Data from 4793 centers were included in this EMR-based study, with a total of 6,722,173 patients. Out of these patients, 427,835 (6.36%) patients were found to have coexistent triple disease (Fig. 1).

### 3.2 Demographic and Other Baseline Characteristics

The mean age (SD) for this group of patients was found to be 59.92 (10.65) years. Most of the cases belonged to the 40–64 year age group ($n = 265,507$; 62.10%) and were males (57.00%). The commonest comorbidities noted besides the triple diseases were coronary artery disease (CAD) (0.40%), hypothyroidism (0.20%), and renal disease (0.20%).

BMI data were available for 113,519 patients. The mean BMI (SD) was noted to be 28.07 (4.84) kg/m$^2$; 27.40% patients had BMI within normal limits, 43.30% patients were pre-obese, 20.90% patients were class 1 obese, 6.30% were class 2 obese, and 2.10% patients were class 3 obese. Only 0.80% had a smoking history.

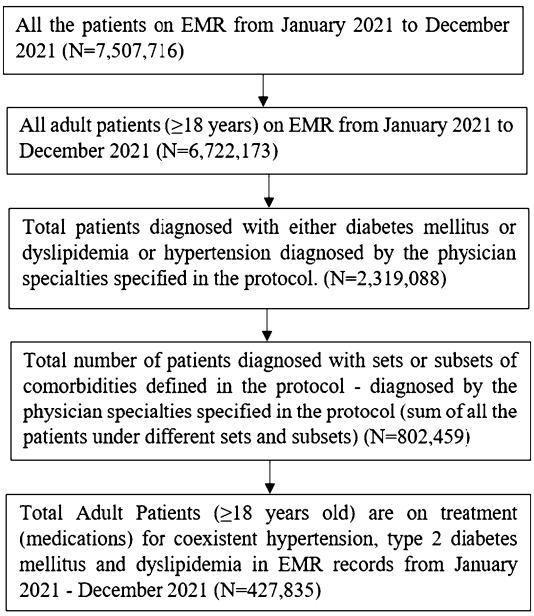


**Fig. 1** CONSORT diagram for patients included in the study. *EMR* electronic medical record, *N* number of patients

Table 1 presents the demographic characteristics of the patients with coexistent triple disease.

### 3.3 Diagnostic Findings

The mean HbA1c for the included patients was noted to be 8.35 ± 1.96 g%, with 27% of patients having HbA1c < 7%. The mean SBP of the patients was 138.81 ± 19.59 mm Hg, while mean DBP was 82.17 ± 10.35 mm Hg: 27.60% patients had SBP <130 mm Hg, while 28.37% patients had DBP below 80 mm Hg. The mean LDL, total cholesterol, and HDL in mg/dl was 98.38 ± 40.39, 174.75 ± 46.73, and 44.5 ± 10.05, respectively, and 55.64% of the patients had serum LDL below 100 mg/dl, 72.03% had serum cholesterol below 200 mg/dl. Overall, 44.15% males and 71.77% females had serum HDL below the normal target range.

Tables 2 and 3 give complete details on the classification of patients based on baseline diagnostic parameters for patients with coexistent triple disease.

### 3.4 Treatment Patterns and Change in Therapy

The most common monotherapy used for managing hypertension was angiotensin receptor blockers (ARB) (24.80%), followed by beta blockers (24.30%), calcium channel blockers (CCB) (15.00%), and diuretics (14.20%). The commonest combinations administered for hypertension were antihypertensives with diuretics (14.30%), followed by ARB plus

**Table 1** Demographic characteristics—patients with coexistent triple disease

| Characteristic (unit) | Patient count *n* (%) |
|---|---|
| **Age groups** | |
| 18–39 years | 12,796 (3.00) |
| 40–64 years | 265,507 (62.10) |
| ≥ 65 years | 149,513 (34.90) |
| **Gender distribution** | |
| Male | 243,715 (57.00) |
| Female | 184,083 (43.00) |
| **Three commonest comorbidities** | |
| CAD | 1919 (0.40) |
| Hypothyroidism | 780 (0.20) |
| Renal disease | 719 (0.20) |
| **Obesity** | |
| Normal (BMI 18.5–24.99) | 30,988 (27.40) |
| Pre-obese (25–29.99) | 49,023 (43.3) |
| Class 1 (BMI 30–34.99) | 23,657 (20.9) |
| Class 2 (BMI 35–39.99) | 7157 (6.30) |
| Class 3 (BMI ≥ 40) | 2407 (2.10) |

*BMI* body mass index, *CAD* coronary artery disease, *n* number of patients

**Table 2** Classification based on baseline diagnostic parameter (BP and blood sugar)—patients with coexistent triple disease

| Parameter | Patient count (%) |
|---|---|
| **Systolic BP (*n* = 345,314)** | |
| < 120 mm Hg | 37,734 (10.93) |
| 120–130 mm Hg | 57,547 (16.67) |
| 130–140 mm Hg | 79,315 (22.97) |
| 140–180 mm Hg | 155,822 (45.13) |
| ≥ 180 mm Hg | 148,96 (4.32) |
| **Diastolic BP (*n* = 343,660)** | |
| < 80 mm Hg | 97,492 (28.37) |
| 80–90 mm Hg | 150,151 (43.7) |
| 90–120 mm Hg | 94,671 (27.55) |
| ≥ 120 mm Hg | 1346 (0.4) |
| **HbA1c (*n* = 107,576)** | |
| < 5.7% | 2367 (2.21) |
| 5.7–6.5% | 13,143 (12.22) |
| 6.5–7% | 13,152 (12.23) |
| 7–8% | 26,238 (24.4) |
| 8–9% | 18,885 (17.56) |
| 9–10% | 12,794 (11.9) |
| ≥ 10% | 20,997 (19.52) |
| **RBS (*n* = 52,027)** | |
| < 200 mg/dl | 26,889 (51.69) |
| ≥ 200 mg/dl | 25,138 (48.32) |
| **FBS (*n* = 131,948)** | |
| < 126 mg/dl | 52,954 (40.14) |
| ≥ 126 mg/dl | 78,994 (59.87) |
| **PPBS (*n* = 116,196)** | |
| < 200 mg/dl | 54,606 (47) |
| ≥ 200 mg/dl | 61,590 (53) |

*BP* blood pressure, *FBS* fasting blood sugar, *HbA1c* glycated hemoglobin, *n* number of patients, *PPBS* postprandial blood sugar, *RBS* random blood sugar

CCB (13.30%), ARB plus beta blocker (7.70%), and CCB plus beta blocker (7.00%).

For dyslipidemia, the majority of patients (56.60%) had received combination of lipid lowering drugs with drugs for other comorbid conditions, while 38.60% cases had received plain statins.

The most common class of antidiabetic drug class prescribed to patients were biguanides (74.60%), followed by combination of biguanide and sulphonylurea (41.00%), biguanide and dipeptidyl-peptidase 4 (DPP 4) inhibitors (29.40%), DPP4 inhibitors monotherapy (22.90%), insulin (19.80%), sodium–glucose cotransporter-2 (SGLT-2) inhibitors (18.10%), and alpha-glucosidase inhibitors (AGI) (18%).

The most common medications prescribed for cardiac comorbidity included anticoagulants (14.90%), vasodilators (8.50%), other anti-anginal agents (4.10%), and antiarrhythmic agents (1.20%). Nitrates were used for a very small proportion of patients (0.60%).

Figure 2 shows the treatment details of patients included in study with coexistent triple disease.

## 4 Discussion

In present study, the prevalence of coexistent triple disease was noted to be 6.36%. A study from China had noted that 2.33% of the participants had hypertension, T2DM, and dyslipidemia at the same time [14]. The prevalence of hypertension, T2DM, and dyslipidemia continues to rise globally. A key reason behind the rising trend is lifestyles associated with low energy expenditure and high calorie intake, particularly in lower-income and developing countries.

It is predicted that the number of cases of T2DM will rise from 415 million to 642 million by 2040 [15]. Scientific literature shows that the main factors driving the T2DM epidemic in both urban and rural areas of India are obesity, age, and family history of T2DM. Some studies have identified male gender as an independent risk factor for T2DM, other studies have shown conflicting results [16]. In the present study, the majority of cases were males (57%), with most belonging to pre-obese subgroup, while 62.10% of the patients were between 40 and 64 years of age. Since the majority belonged to the economically productive age group, the triple disease also has a definite economic impact for

**Table 3** Classification based on baseline diagnostic parameters (lipid profile and serum creatinine)—patients with coexistent triple disease

| Parameter | Patient count (%) |
|---|---|
| **Serum LDL–cholesterol (*n* = 55,114)** | |
| < 30 mg/dl | 711 (1.30) |
| 30–40 mg/dl | 1628 (2.96) |
| 40–55 mg/dl | 5089 (9.24) |
| 55–70 mg/dl | 7309 (13.27) |
| 70–100 mg/dl | 15,909 (28.87) |
| 100–130 mg/dl | 12,453 (22.60) |
| 130–160 mg/dl | 7799 (14.16) |
| 160–190 mg/dl | 3035 (5.51) |
| ≥ 190 mg/dl | 1181 (2.15) |
| **Serum total cholesterol (*n* = 13,918)** | |
| < 200 mg/dl | 10,024 (72.03) |
| 200–240 mg/dl | 2518 (18.10) |
| ≥ 240 mg/dl | 1376 (9.89) |
| **Serum triglycerides (*n* = 55,041)** | |
| < 150 mg/dl | 24,035 (43.67) |
| 150–200 mg/dl | 13,205 (24) |
| 200–500 mg/dl | 17,801 (32.35) |
| **VLDL cholesterol (*n* = 25,367)** | |
| ≥ 30 mg/dl | 10,431 (41.13) |
| < 30 mg/dl | 14,936 (58.88) |
| **Serum HDL–cholesterol (male) (*n* = 29,540)** | |
| < 40 mg/dl | 13,040 (44.15) |
| 40–60 mg/dl | 15,228 (51.56) |
| ≥ 60 mg/dl | 1272 (4.31) |
| **Serum HDL–cholesterol (female) (*n* = 22,906)** | |
| < 50 mg/dl | 16,438 (71.77) |
| 50–60 mg/dl | 4349 (18.99) |
| ≥ 60 mg/dl | 2119 (9.26) |
| **Serum creatinine (male) (*n* = 50,567)** | |
| < 0.7 mg/dl | 2249 (4.45) |
| 0.7–1.3 mg/dl | 33,597 (66.45) |
| ≥ 1.3 mg/dl | 14,721 (29.12) |
| **Serum creatinine (female) (*n* = 36,106)** | |
| < 0.5 mg/dl | 556 (1.54) |
| 0.5–1.1 mg/dl | 26,206 (72.59) |
| ≥ 1.1 mg/dl | 9344 (25.88) |

*HDL* high-density lipoprotein, *LDL* low-density lipoprotein, *n* number of patients, *PPBS* postprandial blood sugar, *RBS* random blood sugar, *VLDL* very low-density lipoprotein

the patients and their families. Only 0.80% of cases had a smoking history, which is consistent with some similar findings in a previous study from Chennai, India [17]. Obesity was identified in 29.30% of the patients, while pre-obesity was identified in 43.30%. This is an indicator, in line with scientific evidence, about the role of obesity as a risk factor in development of triple disease components [10]. This also highlights the importance of lifestyle modification, which can curb obesity and decrease the risk of triple disease.

Seventy-four percent of patients in present study had HbA1c > 7%, 59.87% of the recorded patients with triple comorbidity were noted to have fasting blood sugar (FBS) ≥ 126 mg/dl, and 53% patients had postprandial blood sugar (PPBS) of ≥ 200 mg/dl. Hence, the problem of uncontrolled T2DM cannot be neglected, since a high proportion of cases in present study pointed toward high glycemic parameters. In a study done by Mahapatra et al., the prevalence of uncontrolled diabetes was noted to be 46.43%, while another study by Kanungo et al. found the prevalence of uncontrolled T2DM to be 47% [18, 19]. Nonadherence to medications and limited resources to monitor the blood glucose levels in certain government infrastructure can contribute to the high proportion of uncontrolled cases.

Hypertension is noted to be more common than T2DM, with a recent worldwide estimate of 1.39 billion cases [20]. In the present study, 49.45% of patients with triple comorbidity showed SBP above the normal range, and 27.59% of patients had DBP above the normal range. This points to the high proportion of uncontrolled hypertension in the country. According to a recently published meta-analysis in the Lancet, it has been noted that more than 75% of Indian hypertensive patients do not have their blood pressure in control. The same meta-analysis also mentioned that treatment adherence and access to medicine are key determinants of blood pressure control [21]. A study conducted in South India revealed that stress, poor lifestyle, and poor health-seeking behavior, along with other factors such as diet and exercise lead to poor control of diabetes and hypertension [22]. Another study showed that individuals aged above 60 years with increased duration of diabetes were also one of the main causes of uncontrolled BP [23]. Dyslipidemia was also discovered in the current study, which is consistent with an Indian study by Joshi et al., which examined a large sample of 16,607 cases. The same reference study also noted that 13.90% enrolled cases had hypercholesterolemia, 29.50% had hypertriglyceridemia, 72.30% had low HDL, 11.80% had high LDL levels, and 79% had abnormalities in one of the lipid parameters [24]. In the present study, more than 35% cases had LDL cholesterol > 100 mg/dl, around 28% had recorded total serum cholesterol > 200 mg/dl, more than 32% had serum triglycerides > 200 mg/dl, and more than 44% of males and 71% of females, respectively, had low serum HDL. In the same study by Joshi et al. discussed above, hypercholesterolemia was strongly and positively associated with age ≥ 60 years, urban residence, high income, overweight, generalized obesity, abdominal obesity, fat and oil intake (above median), T2DM, prediabetes, and hypertension. Hypertriglyceridemia was positively associated with all factors entered in the model, except age ≥ 60 years. Low HDL was positively associated with female

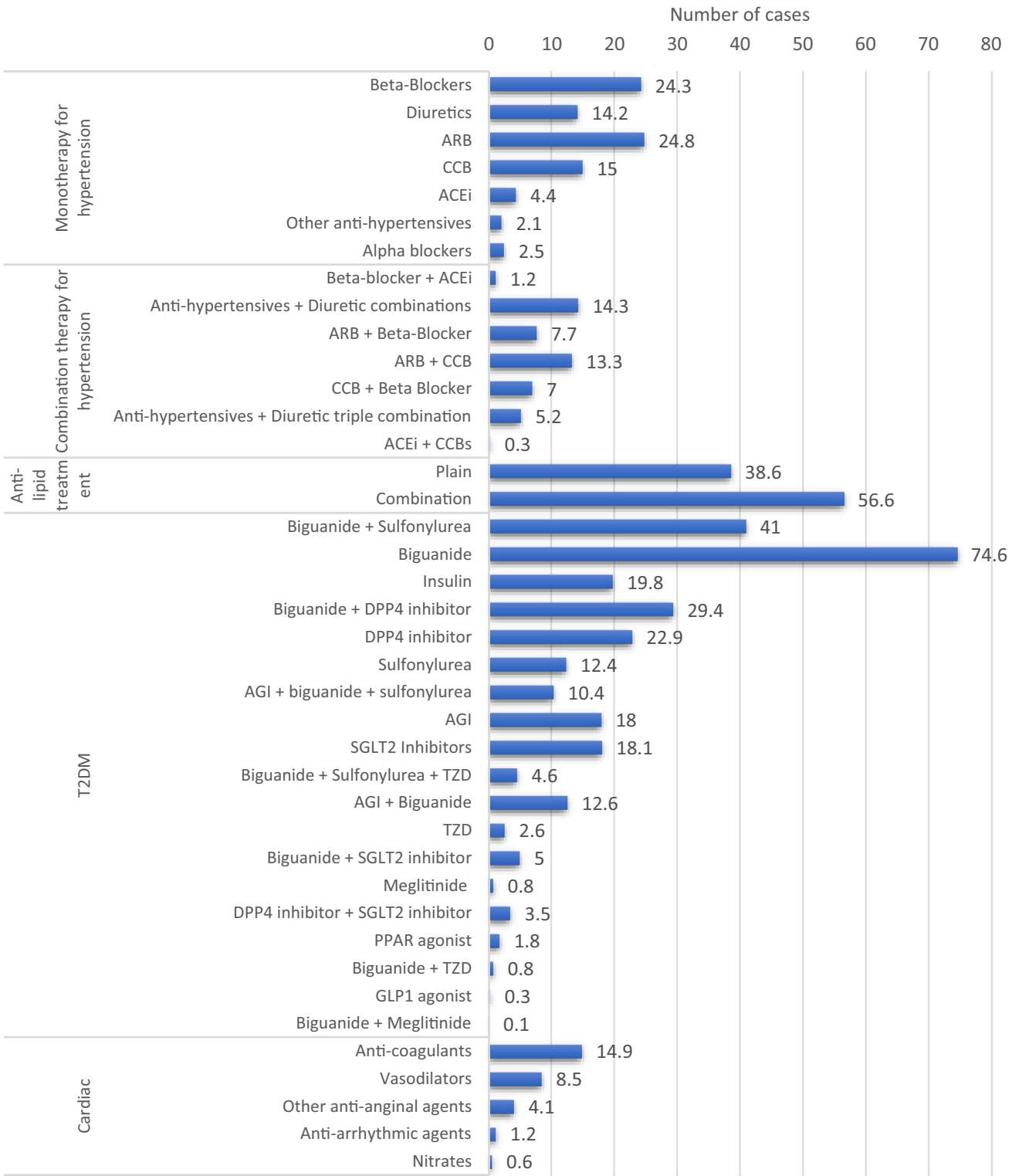


**Fig. 2** Proportion of patients with coexistent triple disease prescribed with various monotherapy and combination therapy. *ACEi* angiotensin converting enzyme inhibitors, *AGI* alpha-glucosidase inhibitors, *ARB* angiotensin receptor blockers, *CCB* calcium channel blockers, *T2DM* type 2 diabetes mellitus, *DPP4* dipeptidyl-peptidase 4, *GLP1* glucagon-like peptide-1, *PPAR* peroxisome proliferator-activated receptor, *SGLT2* sodium–glucose cotransporter-2, *TZD* thiazolidinediones

gender, generalized obesity, abdominal obesity, sedentary lifestyle, and diabetes. High LDL was positively associated with all factors entered in the model and mentioned above. Uncontrolled lipid parameters remain a major problem despite statin usage, with adherence to medications and treatment access being key issues. In addition, lack of regular monitoring of the blood parameters may contribute to the uncontrolled state.

The link between the three comorbid conditions is well established, and the tendency for certain CVD risk factors to cluster, such as obesity, insulin resistance, glucose intolerance, dyslipidemia, and hypertension, has long been recognized and dubbed the metabolic syndrome [25]. The INTERHEART study has shown that individual risk factors enhance the total cardiovascular risk two- to threefold, while the coexistence of triple disease in the same individual (along with other risk factors like smoking) can lead to a 20-time rise in the risk. [26].

Insulin resistance (IR) denotes an impaired response to insulin in skeletal muscle, liver, adipose, and cardiovascular (CV) tissue. IR arises because of various genetic, acquired, and environmental factors, including the presence of obesity, especially central obesity. IR is associated with increased risk of both hypertension and dyslipidemia, pointing out to the strong interplay between the conditions. Additionally, increased oxidized LDL production may be related to hypertension through sympathetic activation and decreased endothelial-dependent nitric oxide (NO) production [27]. IR appears to be a key feature of metabolic syndrome, which is linked to hypertension, hyperlipidemia, hypercoagulability, inflammation, and, eventually, atherosclerosis and CVD [28].

IR is linked to obesity, especially central obesity, although it can also exist in lean people with high BP [29]. Obese persons experience adipocyte hypertrophy with calorie excess, whether in subcutaneous or visceral locations. Visceral adipocytes are more susceptible to cellular death as they start to expand and have macrophages infiltrate their stromal vascular component [30]. These macrophages produce "crown-like structures" surrounding the dead adipocytes, a histologic feature connected to the production of cytokines and inducible NO synthase [31]. These alterations have been demonstrated to occur simultaneously with the onset of insulin resistance, establishing a pathophysiological connection between vascular and metabolic diseases. [32]. Adipocyte hypertrophy is linked to greater triglyceride storage, a higher lipolytic rate, and an atherogenic and abnormal lipid profile, in addition to these proinflammatory alterations. Endothelial dysfunction, a significant contributor to atherosclerosis and its modulator, is brought on by the proinflammatory and metabolic effects of obesity and insulin resistance. Cell proliferation, hypertrophy, remodeling, and apoptosis are also brought on by the concomitant low-grade inflammation in the vascular wall's smooth muscle and endothelial cells [33].

The pancreas compensates for the tissue's lack of insulin sensitivity in T2DM cases by secreting an excessive amount of the hormone (hyperinsulinemia) to keep the blood glucose levels within a normal range. By working in concert with apolipoprotein B, IR has been demonstrated to be an independent risk factor for ischemic heart disease [34]. Additionally, it foretells the emergence of hypertension, and altered lipoprotein profile [35]. Studies have shown that IR/hyperinsulinemia leads to hypertension through several mechanisms, including sympathetic nervous system activation, increased sodium retention in the renal tubules, elevated intracellular calcium concentrations, and proliferation of vascular smooth muscle cells [36]. There is strong published evidence that people with T2DM have hypertension twice as often as people without the condition [37]. On similar lines, T2DM is roughly 2.5 times more likely to develop in those with hypertension [38]. In turn, hypertension can affect glucose metabolism via a variety of mechanisms. Angiotensin II's overactivity blocks the insulin growth factor-1 (IGF-1) signaling pathway, which in turn impairs the functions of IGF-1 and insulin as a vasodilator and glucose transporter. Inhibited IGF-1 and insulin can worsen vasoconstriction by impairing sodium pump action, endothelial nitric oxide synthase activity, and nitric oxide metabolism [39]. Dyslipidemia is a known risk factor for CVD, and when it coexists with hypertension and T2DM, the risk of CVD rises by 75% and further increases morbidity and mortality [40–42]. The development of CVD, which is the main cause of early death in T2DM patients, is eventually brought on by the clustering of risk factors in this population. Other CVD risk variables such as microalbuminuria, central obesity, IR, hypercoagulation, elevated inflammation, and left ventricular hypertrophy cluster with hypertension in T2DM patients.

In patients with triple disease, 29.12% of males and 25.88% of females had serum creatinine above the normal range. Microvascular and macrovascular complications of triple disease can also alter the renal functioning, ultimately leading to aberrant serum creatinine. Diabetic kidney disease (DKD) is typified by persistent albuminuria, arterial blood pressure elevation, a relentless decline in estimated glomerular filtration rate (eGFR), and an accompanying high risk of cardiovascular morbidity and mortality [43]. The process of hypertension in DKD is complicated and not adequately understood; it includes electrolyte imbalance, activation of the renin–angiotensin aldosterone system (RAAS), endothelial cell dysfunction (ECD), and enhanced oxidative stress [44]. Augmented serum creatinine levels were eight times more common in hypertensive individuals (9.10%) than in normotensive cases (1.10%). Additionally, raised serum creatinine was eight times more common in people already on

medication for raised blood pressure compared those not on medication (13.00% versus 1.60%) [45].

In the present study, beta blockers were given to a large proportion of patients, even though they are not considered a first-line treatment option by the India Hypertension Control Initiative guidelines [46]. The use of beta blockers in hypertension has been a matter of debate for a long time. In younger/middle-aged people, high sympathetic nerve activity is the underlying cause of primary/essential hypertension. High resting heart rates and high plasma norepinephrine concentrations (independent of blood pressure) are associated with early cardiovascular events and mortality in this age range. As a result, in this younger age range, diuretics, dihydropyridine calcium blockers, and ARBs are unacceptable first-line options for treating hypertension. In younger (under 60 years old) hypertensive people, beta blockers outperform randomized placebo and other antihypertensive medications in terms of reduced risk of mortality, stroke, and myocardial infarction, and represent a suitable first-line treatment option (certainly in men) [47]. The India hypertension control initiative (IHCI) recommends use of beta blockers in patients with a history of a heart attack within the last 3 years or atrial fibrillation or heart failure. Beta blockers are used more frequently in the present study as patients have other comorbid conditions along with HTN such as T2DM and dyslipidemia, which increases risk of cardiovascular disease where beta blockers could be beneficial [48].

The present study, which demonstrates that coexistence of triple disease is common, underlines the importance of screening patients for all three chronic conditions together. If anyone is missed, then the aggravated chances of CVD will be overlooked, putting the patient at risk. The estimation of the prevalence of hypertension, T2DM, and dyslipidemia will ensure proper planning of health care resources for both primary and secondary prevention of CVDs. However, it is important to note that due to the heterogeneous nature of the Indian population, there may be potential confounding factors such as regional differences in patient characteristics, lifestyle, and socioeconomics, which may impact the evaluated prevalence in the study. Even though data of a large set of population was evaluated, the cross-sectional nature of the study makes the findings suggestive rather than causal. Hence, the findings of this study should be interpreted with caution.

There are various obstacles for managing this important cohort of "triple disease." Health system barriers include inadequate care accessibility, poor integration between primary care clinics and local hospitals, lack of resources, and neglect of adult chronic disease. Health care provider–related barriers are inadequate training of hospital staff, lack of availability or reluctance to adopt Clinical Practice Guidelines, and lack of counseling prioritization. User-related barriers for treatment adherence include lack of accurate information, resistance to adopt lifelong treatment, affordability, and medical advice mistrust. These obstacles can be opportunities to enhance the outcomes of the high-risk "triple disease" cohort.

The study had a few limitations. Since the study was an EMR database analysis, some of the challenges of the study design included missing data of patients. Due to the nature of study design the evaluation of complexities of disease progression and management was not feasible. The study had some selection bias due to the overrepresentation of data from those clinics or centers within the EMR system. Potential confounding factors may have also impacted the final analysis of triple disease prevalence.

## 5 Conclusions

The coexistence of triple disease was observed in over half of the patients included in the study, particularly affecting middle-aged patients classified as pre-obese and obese. Additionally, despite the availability of medications for all three chronic conditions, the rate of uncontrolled cases of hypertension, T2DM, and dyslipidemia remains high in real-world scenarios. This study emphasized the need for a prospective study analyzing treatment outcome in patients with triple disease. These findings also underscore the importance of conducting additional public health policy research to evaluate strategies for implementing early detection and effective disease control. Genome-wide association studies can also play a crucial role in promoting the practice of precision medicine among Indian patients.

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## Declarations

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**Conflict of interest** Dr. Jamshed Dalal, Dr. Praveen Chandra, Dr. Rajeev Chawla, Dr. Viveka Kumar, Dr. Jabir Abdullakutty, and Ms. Snehal Shah declare no conflicts of interest. Dr. Vidhya Natarajan, Dr. Syed Mujtaba Hussain Naqvi, Dr. Kumar Gaurav, Dr. Rahul Rathod, Ms. Gauri Dhanaki, and Dr. Bhavesh Kotak are employees of Dr. Reddy's Laboratories Ltd., which funded the study.

**Availability of data and material** Anonymized and aggregated data is presented in the manuscript.

**Ethics approval** Ethics approval was obtained from the Suraksha Ethics Committee (ECR/644/Inst/MH/2014/RR-20).

**Consent to participate** Informed consent waiver was obtained from the Ethics Committee as this was a non-experimental, retrospective data analysis study.

**Consent for publication** Not applicable.

**Code availability** Not applicable.

**Author contributions** JD, PC, RC, VK, JA, VN, SMHN, KG, RR, GD, and BK contributed to conception, design, manuscript preparation, editing, and review. SS contributed to literature search, data acquisition, data analysis, and manuscript review. All authors have read and approved the final version of manuscript.



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