

# Reproductive Transitions and Cardiometabolic Burden in Type 2 Diabetic Women: A Sri Lankan Cross-sectional Analysis

Piyumi Weerawickrama

piyumik45@gmail.com

General Sir John Kotelawala Defence University

**Chamila Weerasinghe**

General Sir John Kotelawala Defence University

**Anjana Fernando**

General Sir John Kotelawala Defence University

**Dilhara Karunarathna**

General Sir John Kotelawala Defence University

**Chaminda Garusinghe**

Colombo South Teaching Hospital

---

## Research Article

**Keywords:** Cardiovascular risk, Type 2 Diabetes Mellitus, Menopausal women, Reproductive Transitions

**Posted Date:** March 27th, 2026

**DOI:** <https://doi.org/10.21203/rs.3.rs-8067197/v1>

**License:**   This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

**Additional Declarations:** No competing interests reported.

---

# Abstract

**Background:** Cardiovascular disease (CVD) is a leading cause of mortality among women with type 2 diabetes mellitus (T2DM) and remains understudied. This study examined the association between reproductive and metabolic factors with CVD risk in T2DM women.

**Methods & Materials:** CVD risk was assessed in 293 women with T2DM at Colombo South Teaching Hospital using the Framingham Risk Score. Data on CVD risk factors and reproductive history were collected using a pre tested interviewer administered questioner. The demographic parameters and correlations were assessed. Multiple regression analysis was performed to identify the Impact of risk factors.

**Results:** Prevalences observed as follows, dyslipidemia 25.9%, elevated LDL cholesterol 41.3%, hypertriglyceridemia 33.1%, low HDL cholesterol 19.5%, hypertension 54.9%, overweight 50.8%, and central obesity 98.0%. Only 17.06% women achieved the three therapeutic targets (fasting blood sugar, Blood Pressure and blood lipids). The CVD risk was significantly high among postmenopausal women than premenopausal women ( $p < 0.001$ ). Menopause status, gestational diabetes mellitus, use of hormonal contraceptives and age at menopause were significantly correlated with the CVD risk ( $p < 0.001$ ). The multiple linear regression analysis showed that menopause status, DBP, LDL/HDL ratio and time since menopause were significant contributors to CVD risk in the Study Population ( $p < 0.001$ ). Among the postmenopausal group, DBP, LDL/HDL ratio, and time since menopause were found to be significant contributors for CVD risk ( $p < 0.001$ ).

**Conclusion:** Postmenopausal women with T2DM face a significantly higher CVD risk in studied Sri Lankan population, with DBP, LDL/HDL ratio, and time since menopause identified as key contributors. Poor achievement of therapeutic targets highlights the need for targeted interventions to manage CVD risk in this population.

**Ethical Clearance:** This study received approval from the Ethical Review Committee of Colombo South Teaching Hospital (Application No:986).

## Background

Cardiovascular diseases (CVD), a group of disorders that involves of heart and blood vessels includes hypertension (high blood pressure), coronary heart disease (heart attack), cerebrovascular disease (stroke), peripheral vascular disease, heart failure, congenital heart disease, rheumatic heart disease & cardiomyopathies. CVDs are the primary cause of mortality, accounts for one-third of deaths globally [1]. In Sri Lanka, the prevalence of CVDs has surged over the past few decades, making them the leading cause of death for the last 40 years [2] Therefore, CVDs place a substantial social and economic burden on Sri Lanka.

Type 2 Diabetes Mellitus (T2DM) is recognized as a major risk factor for developing CVDs. Numerous studies have demonstrated that individuals with T2DM have a higher risk of CVD compared to age and sex

matched healthy individuals[3] As reported by Arambewela *et al.*, 2018 there's a high prevalence of CVDs among patients with T2DM in Sri Lanka [4]. Therefore, CVD is considered as a leading cause for mortality and morbidity among patients with T2DM in Sri Lanka. CVDs accounts for one third of all deaths among women and also when compared with men, women with Diabetes mellitus (DM) have higher mortality rate[5]. Estrogen is widely recognized for its protective role against cardiovascular complications in non-menopausal women, when compared to age-matched men[6]. Therefore, women with a regular menstrual cycle have a lower risk of developing CVD than age matched men. However, oxidative stress caused by hyperglycemia impairs the interaction between estrogen and endothelial estrogen receptors, diminishing the hormone's protective effects in women with T2DM[7] . Moreover, many studies have proven that the postmenopausal women are having a greater risk of developing CVD when compared to women in the reproductive age due to marked decreased ovarian estrogen secretion during the menopause transition [8].Furthermore, elevation of LDL-C and reduction of HDL-C after menopause might further aggravate the CVD risk among menopausal women. In addition to the known major risk factors, some studies have reported that several reproductive factors which determine the level and duration of exposure to endogenous estrogen including age at menopause, time since menopause and total reproductive years act as risk factors for development of CVD among women with T2DM [9][10]Use of hormonal contraceptives also a considerable risk factor of developing CVDs among women [11]. Moreover, some studies have proven that it is important to consider parity and duration of breast feeding when assessing the CVD risk among women [12]. In addition, pregnancy complication such as gestational diabetes and pregnancy induced hypertension may increase the risk of developing CVDs among women[13].

The assessment of CVD risk in patients with T2DM is essential for initiating primary preventive strategies aimed at reducing future cardiovascular complications. Over the past two decades, several risk assessment tools have been developed, including the Framingham Risk Score (FRS), the UK Prospective Diabetes Study (UKPDS) risk engine, and the WHO/International Society of Hypertension (WHO/ISH) risk prediction charts. The FRS, originally developed in North America, was validated as a tool to assess CVD risk in Caucasian populations. Over time, it has been adapted and validated for use in other regions, including several countries in Asia, demonstrating strong performance [14–16]. The FRS is designed to predict an individual's 10-year CVD risk for those aged  $\geq 30$  years, factoring in total cholesterol levels, HDL-C levels, systolic blood pressure, smoking status, and the presence or absence of diabetes. The score is also adjusted for the individual's age and gender [17]. Even though several studies have been done in different parts of the world to assess the CVD risk in women with DM and its association with reproductive factors, it has not been well assessed in Sri Lanka. Further The Lancet Women and Cardiovascular Disease Commission, aiming to reduce the global burden by 2030, aptly stated that “cardiovascular disease in women remains understudied, under-recognized, underdiagnosed, and undertreated.”[18]. Therefore, it is important to determine the total risk of developing CVDs and its association with different reproductive factors to set the guidelines to reduce future cardiovascular events in Sri Lankan women with T2DM.

## Methodology

## Study Participants

This cross-sectional study was conducted at the Diabetic and Endocrinology Unit of Colombo South Teaching Hospital (CSTH). From the cohort of 343 female patients with T2DM who attended the clinic, 293 were included in the study due to incomplete data for some participants. Written informed consent was obtained from the patients prior to the commencement of the study. This study received approval from the Ethical Review Committee of CSTH (Application No:986).

## Data Collection

Data on socio-demographic and clinical characteristics, such as age, reproductive history, smoking status, family history of diabetes mellitus (DM) and CVDs were collected using interviewer-administered questionnaires and medical records. Biochemical data, including fasting blood sugar (FBS), Total cholesterol, high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) were obtained from routine clinical investigations conducted at the biochemistry laboratory of CSTH. Anthropometric measurements, including height, weight, waist circumference, and hip circumference, were measured by trained investigators following WHO guidelines [19]. Blood pressure measurements, including systolic blood pressure (SBP) and diastolic blood pressure (DBP), were collected by medical officers at the clinic.

## Analysis of CVD risk factors and Calculation of CVD risk.

Dyslipidaemia was defined as meeting any of the following criteria, LDL-C levels  $\geq 130$  mg/dL, triglyceride levels  $\geq 150$  mg/dL, HDL-C levels  $< 40$  mg/dL, or total blood cholesterol level  $\geq 240$  mg/dL. Additionally, individuals on lipid-lowering medications were also considered to have dyslipidaemia [20]. Overweight was defined as a body mass index (BMI)  $\geq 25$  kg/m<sup>2</sup>, and obesity was defined as a BMI  $\geq 30$  kg/m<sup>2</sup> [21]. Central obesity in women was defined as a waist circumference  $> 80$  cm and/or a waist-to-hip ratio (WHR) of  $\geq 0.85$  cm, indicating a substantially increased risk of CVDs [22]. Hypertension was defined as an SBP  $\geq 140$  mmHg, a DBP  $\geq 90$  mmHg, or being a known hypertensive or on antihypertensive medication [23]. Current smokers and patients who had quit smoking less than one year prior to the assessment were considered smokers.

The calculation of CVD risk using the Female FRS is based on six parameters, age, total TC level, HDL-C level, SBP, smoking status, and diabetes status (yes or no). According to the Female FRS, a risk point is assigned for each risk factor category, and the FRS is calculated by summing the risk points for each factor. The CVD risk percentage is then estimated based on the total points [24].

## Statistical Analysis

The study population was classified into three categories based on the menopausal state and time since menopause: pre-menopause, post-menopause  $< 5$  years and post menopause  $\geq 5$  years. SPSS ver.26 (SPSS Inc, Chicago, IL, USA) was used to analyze the data statistically.

All data were expressed as mean ± standard deviation (SD) or percentages. One-way ANOVA (for continuous variables) and Chi-square (for non-parametric variables) was used to compare the data between different categories of FRS. Pearson’s correlation test was used to determine the correlation between CVD risk and associated factors including age, diabetes course, FBS level, lipid profile, BMI, WHR and reproductive factors. Multiple regression analysis was performed for factors which showed statistically significant correlation with CVD risk. The factors which are statistically correlated to CVD risk were considered as independent factors. All statistical tests with p values <0.05 were considered as statistically significant.

## Results

### Prevalence of Known CVD risk factors.

The study population was categorized into three groups based on menopausal status, pre-menopause, post-menopause for less than five years, and post-menopause for five or more years. Dyslipidemia was identified in 25.9% of participants, with the highest prevalence observed in pre-menopausal women (40.8%), exhibiting statistically significant differences between groups ( $\chi^2 = 12.068$ ,  $p = 0.002$ ). Raised LDL levels were present in 41.3% of the population, with pre-menopausal women showing the highest prevalence (50.7%). Hypertriglyceridemia was noted in 33.1% of participants, with the highest occurrence in pre-menopausal women (45.1%), reflecting significant differences between the groups ( $\chi^2 = 10.760$ ,  $p = 0.005$ ). Low HDL levels were found in 19.5% of the population, with the highest prevalence in pre-menopausal women (25.7%). Hypertension was reported in 54.9% of participants, with the highest prevalence in post-menopausal women for less than five years (61.8%). Obesity and overweight, as determined by BMI, were present in 50.8% of the population, with the highest prevalence in post-menopausal women for less than five years (62.5%). Central obesity, as determined by waist-to-hip ratio (WHR), was prevalent in 98.0% of participants, with similar prevalence across the groups: pre-menopausal women (97.2%), post-menopausal women for less than five years (98.2%), and post-menopausal women for five or more years (98.2%). (Table 01)

**Table 01: Prevalence of Known CVD risk factors among three groups based on menopausal state.**

|                            | Total      | Pre-menopause | Post menopause <5y | Post menopause ≥5y | χ <sup>2</sup> | P        |
|----------------------------|------------|---------------|--------------------|--------------------|----------------|----------|
| N                          | 293        | 71            | 56                 | 166                |                |          |
| Dyslipidemia               | 76 (25.9%) | 29 (40.8%)    | 15 (26.8%)         | 32 (19.3%)         | 12.068         | 0.002    |
| Raised LDL                 | 121(41.3%) | 36 (50.7%)    | 22 (39.3%)         | 63 (38.0%)         | 3.452          | 0.178    |
| Hypertriglyceridemia       | 97 (33.1%) | 32 (45.1%)    | 23 (41.1%)         | 42 (25.3%)         | 10.760         | 0.005    |
| low HDL                    | 57 (19.5%) | 18 (25.7%)    | 9 (16.4%)          | 30 (17.9%)         | 2.187          | 0.335    |
| Hypertension               | 161(54.9%) | 30(42.9%)     | 34(61.8%)          | 97(57.7%)          | 5.711          | 0.058    |
| Obesity & Overweight (BMI) | 149(50.8%) | 36(50.7%)     | 35 (62.5%)         | 78 (47.0%)         | 6.429          | 0.169    |
| central Obesity (WHR)      | 287(98.0%) | 69 (97.2%)    | 55 (98.2%)         | 163 (98.2%)        | 0.276          | 0.871[1] |

#### Demographic, clinical characteristics and Biochemical Parameters.

The variables considered are age (55.05 ± 7.56), family history of DM 63.1% (n=185), family history of CVD 33.1% (n=97), diabetes course (months) 119.11 ± 91.15, Weight 60.96 ± 12.00, BMI 26.22 ± 5.57, WHR 9.94 ± 0.05, FBS (mg/dl) 144.00 ± 57.10, total cholesterol (mg/dl) 176.70 ± 43.38, LDL Cholesterol (mg/dl) 99.19 ± 36.89, Triglyceride (mg/dl) 137.82 ± 59.48, HDL (mg/dl) 49.85 ± 14.99, Total Cholesterol/ HDL ratio 3.69 ± 1.00 and LDL/HDL ratio 2.08 ± 0.83 and smoking 0% (n=0). Most of the patients were taking treatments to control T2DM and other associated risk factors including hypertension and dyslipidemia. Oral Hypoglycemic agents 93.6% (n=283), Hypoglycemic agent (insulin) 29% (n=85), anti-hypertensive drugs 63.1% (n=185) and lipid modulators 79.2% (n=232). (Table 02)

**Table 02: Distribution of Demographic, clinical characteristics and Biochemical Parameters.**

| Variable                  | N   | mean $\pm$ SD or percentage |
|---------------------------|-----|-----------------------------|
| Age (Y)                   | 293 | 55.05 $\pm$ 7.56            |
| Family history of DM (%)  | 293 | 185 (63.1%)                 |
| Family history of CVD     | 293 | 97 (33.1%)                  |
| Diabetes course (months)  | 293 | 119.11 $\pm$ 91.15          |
| Weight (kg)               | 293 | 60.96 $\pm$ 12.00           |
| BMI                       | 293 | 26.22 $\pm$ 5.57            |
| WHR                       | 293 | 0.94 $\pm$ 0.05             |
| FBS (mg/dl)               | 293 | 144.00 $\pm$ 57.10          |
| Total cholesterol (mg/dl) | 293 | 176.70 $\pm$ 43.38          |
| LDL (mg/dl)               | 293 | 99.19 $\pm$ 36.89           |
| TG (mg/dl)                | 293 | 137.82 $\pm$ 59.48          |
| HDL (mg/dl)               | 293 | 49.85 $\pm$ 14.99           |
| T- CHOL/HDL Ratio         | 293 | 3.69 $\pm$ 1.00             |
| LDL/HDL Ratio             | 293 | 2.08 $\pm$ 0.83             |
| Oral Hypoglycemic agents  | 293 | 283 (93.6%)                 |
| Insulin                   | 293 | 85 (29%)                    |
| Antihypertensive drugs    | 293 | 185 (63.1%)                 |
| Lipid modulators          | 293 | 232 (79.2%)                 |
| Smoking                   | 293 | 0(0%)[2]                    |

## Reproductive factors

Reproductive factors, age at menarche (years) 13.3  $\pm$  2.78, age at menopause (years) 48.80 $\pm$  4.75, use of hormonal contraceptive 30.0% (88/293), Parity 2.01 $\pm$  0.99, duration of breastfeeding (months) 5.46 $\pm$  36.14, presence of gestational diabetes 21.5% (63/268), presence of gestational hypertension 12.3% (38/268), duration of breastfeeding (months) 53.16  $\pm$ 36.14 and time since menopause(months) 9.43 $\pm$  9.00.(Table 03)

**Table 03: Distribution of Reproductive factors**

| Reproductive factor                      | N   | mean $\pm$ SD or percentage |
|------------------------------------------|-----|-----------------------------|
| Age at menarche (years)                  | 293 | 13.3 $\pm$ 2.78             |
| Menopause age (years)                    | 222 | 48.80 $\pm$ 4.75            |
| Use of hormonal contraceptives (%)       | 293 | 88 (30.0%)                  |
| Parity                                   | 293 | 2.01 $\pm$ 0.99             |
| Duration of breastfeeding (months)       | 267 | 53.46 $\pm$ 36.14           |
| Presence of gestational diabetes (%)     | 268 | 63 (21.5%)                  |
| Presence of gestational hypertension (%) | 268 | 38 (12.3%)                  |
| Time since menopause (months)            | 222 | 9.43 $\pm$ 9.00             |

### FRS risk score and 10-year risk of developing CVD

FRS risk score and 10 years risk of CVD were 15.23 $\pm$ 3.76 and 15.73 $\pm$  7.64 respectively. There was a statistically significant difference in both FRS risk score and the 10-year risk of CVD among non-menopause, post menopause<5 years and post menopause >5 women. There was a tendency of increasing FRS score and 10-year CVD risk with the Age ( $p<0.001$ ). The highest FRS and 10-year CVD risk was observed among the post menopause >5 years subjects (Table 04).

***Table 04: 10 years risk of CVD among the study population and three groups based on menopausal state.***

| Group              | N   | Framingham Risk score     | 10 years risk of CVD<br>Corresponding to FRS % |
|--------------------|-----|---------------------------|------------------------------------------------|
| Pre-menopause      | 71  | 12.51 ±3.27 <sup>bc</sup> | 10.43 ±5.34 <sup>bc</sup>                      |
| Post menopause<5y  | 56  | 15.04 ±3.69 <sup>ac</sup> | 15.14 ±7.34 <sup>ac</sup>                      |
| Post menopause ≥5y | 166 | 16.42 ±3.36 <sup>ab</sup> | 18.13 ±7.43 <sup>ab</sup>                      |
| Total              | 293 | 15.23 ±3.76               | 15.73 ±7.64                                    |
| F                  |     | 32.657                    | 30.355                                         |
| <i>P</i> *         |     | <0.001                    | <0.001                                         |

a Compared with the premenopausal group,  $P < 0.05$ .

b Compared with the postmenopause < 5 y group,  $P < 0.05$ .

c Compared with the postmenopausal ≥5 y group,  $P < 0.05$ .

\* Compared among groups

### Correlation between FRS score and reproductive and Metabolic Risk factors

Correlations between CVD risk (dependent variable) and independent variables which are not included in the FRS risk score such as LDL cholesterol, DBP, FBS, total cholesterol /HDL ratio, LDL/HDL ratio, Triglyceride, Diabetes course, BMI, WHR, age at menarche, menopausal state, age at menopause, Parity, Gestational DM, Gestational hypertension, and use of hormonal contraceptive. The analysis revealed both positive and negative correlations between the CVD risk and various reproductive and metabolic risk factors. Positive correlations were observed between the FRS score and LDL cholesterol ( $r = 0.170$ ,  $p = 0.004$ ), total cholesterol/HDL ratio ( $r = 0.263$ ,  $p < 0.001$ ), LDL/HDL ratio ( $r = 0.235$ ,  $p < 0.001$ ), diastolic blood pressure (DBP) ( $r = 0.336$ ,  $p < 0.001$ ), menopausal status ( $r = 0.417$ ,  $p < 0.001$ ), and age at menopause ( $r = 0.146$ ,  $p = 0.030$ ), suggesting that higher values of these factors are associated with increased cardiovascular risk. In contrast, negative correlations were found with fasting blood sugar (FBS) ( $r = -0.120$ ,  $p = 0.039$ ), gestational diabetes ( $r = -0.182$ ,  $p = 0.003$ ), and the use of hormonal contraceptives ( $r = -0.159$ ,  $p = 0.006$ ). All the variables found to be correlated with FRS score included in the multiple linear regression model except for those which do not meet the requirements of multi co-linearity test (Table 05).

**Table 05: Correlation between FRS score and reproductive and Metabolic Risk factors among study population.**

| VARIABLE                      | n   | Pearson Correlation R | Sig. (2-tailed) P |
|-------------------------------|-----|-----------------------|-------------------|
| FBS                           | 293 | -0.120*               | 0.039             |
| LDL                           | 292 | 0.170**               | 0.004             |
| T. CHOL/HDL                   | 292 | 0.263**               | <0.001            |
| LDL/HDL                       | 292 | 0.235**               | <0.001            |
| DBP                           | 293 | 0.336**               | <0.001            |
| Menopause or not              | 293 | 0.417**               | <0.001            |
| Age at Menopause              | 222 | 0.146*                | 0.030             |
| Gestational DM                | 268 | -0.182**              | 0.003             |
| Use of hormonal contraceptive | 293 | -0.159**              | 0.006[3]          |

**\*\*.** Correlation is significant at the 0.001 level (2-tailed).

**\*.** Correlation is significant at the 0.05 level (2-tailed).

#### **Association of contributory factors with CVD risk among study population.**

FRS score was the dependent variable and menopausal state, LDL cholesterol, LDL/HDL ratio, FBS, DBP, use of hormonal contraceptive, history of gestational DM and time since menopause were the independent variables of the Multiple regression model. FRS score was found to be positively correlated with the menopausal state (yes or no), LDL/ HDL ratio, DBP and time since menopause. ( $\beta$  values 2.861, 1.633, 0.136 and  $-0.119$  respectively,  $p = < 0.001$  which may explain the variance of 41.6%. And the independence of the observation has been met (Durbin Watson =1.894) and ratio with ( $F = 283$ ) = 25.191,  $p < 0.0005$  the prediction of the dependent variable by the independent variable is statistically significant. Accordingly, menopausal state, diastolic blood pressure, LDL/HDL ratio and time since menopause were found to be the independent risk factors for the 10-year CVD risk calculated by FRS for all the patients (Table 06).

**Table 06: Stepwise multiple linear regression for CVD risk and contributory factors among all subjects.**

(n=292)

| variable                | Unstandardized coefficients<br>B | standardized coefficients<br>$\beta$ | T     | P<br>value |
|-------------------------|----------------------------------|--------------------------------------|-------|------------|
| Menopause or not        | 2.861                            | 0.325                                | 5.612 | <0.001     |
| DBP                     | 0.136                            | 0.340                                | 7.340 | <0.001     |
| LDL/HDL Ratio           | 1.633                            | 0.362                                | 4.510 | <0.001     |
| Time since<br>menopause | -0.119                           | 0.224                                | 3.950 | <0.001     |

$$R^2 = 0.416$$

### Association of contributory factors with CVD risk among post-menopausal sub population.

Among postmenopausal women, FRS score was the dependent variable and the independent variables included in the regression model were LDL cholesterol, LDL/HDL ratio, FBS, DBP, use of hormonal contraceptive, gestational DM and time since menopause. FRS score was found to be positively correlated with DBP, LDL/HDL ratio and time since menopause. ( $\beta$  =0.129, 1.878 and 0.115 respectively,  $p < 0.001$ ) which may explain the variance of 30.2% and the independence of the observation has been met (Durbin Watson = 1.906) F ratio with  $F = 7, 214) = 13.129$ ,  $p < 0.0005$ . The prediction of the dependent variable by the independent variables was statistically significant (Table 07).

**Table 07: Stepwise multiple linear regression for CVD risk and contributory factors among postmenopausal sub population.**

(n=222)

|                         | Unstandardized coefficients<br>B | Standardized coefficients<br>$\beta$ | T     | P<br>value |
|-------------------------|----------------------------------|--------------------------------------|-------|------------|
| Diastolic BP            | 0.129                            | 0.353                                | 6.083 | <0.001     |
| LDL/HDL Ratio           | 1.878                            | 0.418                                | 4.497 | <0.001     |
| Time since<br>menopause | 0.115                            | 0.221                                | 3.726 | <0.001     |

$$R^2 = 0.302$$

## Discussion

The socio-demographic and clinical characteristics of the study participants were consistent with those observed in similar studies conducted in Sri Lanka among individuals with T2DM. The mean age of the participants was  $55.05 \pm 7.56$  years, with a notable 63.1% (n=185) reporting a family history of DM, and 33.1% (n=97) having a family history of CVD. The average duration of diabetes was  $119.11 \pm 91.15$  months, indicating a population with a relatively long history of managing the condition. In terms of clinical

measures, the mean weight was  $60.96 \pm 12.00$  kg, and the average BMI was  $26.22 \pm 5.57$  kg/m<sup>2</sup>, which is classified as overweight according to standard BMI categories. Furthermore, the mean WHR was  $0.94 \pm 0.05$ , reflecting central adiposity, a known risk factor for cardiovascular events. The mean FBS was  $144.00 \pm 57.10$  mg/dl, and lipid profile analysis revealed a mean total cholesterol level of  $176.70 \pm 43.38$  mg/dl, with LDL cholesterol averaging  $99.19 \pm 36.89$  mg/dl, and triglycerides at  $137.82 \pm 59.48$  mg/dl. The mean HDL cholesterol level was  $49.85 \pm 14.99$  mg/dl, and the mean total cholesterol/HDL ratio was  $3.69 \pm 1.00$ , with a mean LDL/HDL ratio of  $2.08 \pm 0.83$ . Notably, none of the participants reported smoking (0%, n=0), which is a positive health indicator in the context of cardiovascular risk. These findings suggest a population at heightened risk for both diabetes-related complications and cardiovascular diseases. [4, 25].

Even though 93.6% of patients were under oral hyperglycemic agents and 29% were under insulin therapy, the mean of FBS was beyond the clinical cut off value,  $144.00 \pm 57.10$  mg /dl. This study was conducted during Covid pandemic thus, the high mean FBS, despite the use of hypoglycemic therapy, may be attributed to limited access to medications and reduced clinical attention as a result of the COVID-19 pandemic. A study conducted in 2010 among T2DM patients in Sri Lanka reported that  $0.83 \pm 0.09$ cm mean waist to hip ratio in female subjects in western province and present study indicated  $0.94 \pm 0.05$ cm mean of waist to hip ratio This difference in the waist to hip ratio clearly depicts the negative impact of changes happened to the life styles during past decade [26]. Despite a high prevalence of known risk factors in the studied population, a substantial proportion of patients were receiving antihypertensive medications (63.1%) and lipid-lowering agents (79.2%). This apparent discrepancy may be influenced by several factors, including suboptimal adherence to prescribed treatments, unhealthy dietary patterns, sedentary lifestyles, and reduced clinical oversight during the COVID-19 pandemic.

It is well established that estrogen provides a protective effect against CVD in healthy, non-menopausal women by regulating LDL cholesterol levels. [8]. However, the current study revealed a significantly higher prevalence of dyslipidemia, elevated LDL, hypertriglyceridemia, and low HDL among premenopausal women compared to postmenopausal women. This may be due to the diminished protective effects of estrogen resulting from metabolic changes associated with T2DM, which are further exacerbated by poor adherence to prescribed treatments and unhealthy lifestyle choices [7].

A similar study conducted among patient with T2DM in Sri Lanka reported prevalence of major CVD risk factors: raised LDL cholesterol (44.7%); hypertriglyceridemia, (26.5%); low HDL(65.5%);overweight and obesity(78.8%), hypertension (77.6%) and smoking (0.6%) [4]. According to the results of the present study 50.8% of women were overweight/obese and 98.0% were with central obesity. Moreover, the central obesity was seen among all the three groups irrespective of the reproductive state. According to the study conducted by Arambewela et al, 2018 in Sri Lanka, the prevalence of obesity/overweight was 75.7% which is higher than the prevalence observed by the current study. This difference may be due to the difference of study population as the past study recruited patients with all diabetes related complications and CVD and present study excluded the patients with history of CVD. However, the prevalence of high LDL (41.3%), triglyceridemic (33.1%) and smoking (0%) reported by the present study is comparatively similar to the prevalence reported by the previous study [4].

This study found that the risk of CVD is significantly higher in postmenopausal women compared to premenopausal women. Similarly, *Yang et al, 2019* reported that postmenopausal women have a notably increased risk of both fatal and non-fatal CVD compared to their premenopausal counterparts. [27]

According to the present study, menopausal status, LDL cholesterol level, age at menopause, history of gestational DM, use of hormonal contraceptives found to be correlated with CVD risk score. *Yang et al* revealed that when compared with women who experienced menopause at 48 to 50 years, women with lower menopausal age (< 43 years) had a higher risk of mortality due to CVDs [27]. The present study did not show any significant association between CVD risk and history of gestational hypertension. However, a study conducted by *Riise et al., 2018* revealed that there was a significant relationship between CVD risk and history of gestational hypertension[28]. The results of the current study are consistent with the findings of *Tobias et al.,2017*, which demonstrated an increased risk of cardiovascular diseases (CVDs) among women who had gestational diabetes mellitus. [13]. Present study did not show any association between duration of breastfeeding and CVD risk. In contrast, *Peters et al., 2016* revealed that breastfeeding is associated with low cardiac risk[29].

According to the multiple regression analysis, the contributing factors for high CVD risk among post-menopausal women were DBP, LDL/HDL and time since menopause. A similar study conducted in China reported that LDL cholesterol, FBG and time since menopause were the contributing factors for CVD risk among post-menopausal women.[30] In our study FBS was not identified as a contributing factor but the study conducted in China revealed that high FBS is a contributing factor for high CVD risk. It may be due to the ethnic difference of the study population.

This study has several limitations. Since the research was conducted among women with T2DM attending the diabetes and endocrinology clinic at CSTH, the findings may not be generalizable to broader populations in Sri Lanka due to the single-center study design. Additionally, the assessment tools used for evaluating CVD risk were not specifically designed for individuals with diabetes, which may have affected the accuracy of risk estimation. The reliance on self-reported reproductive data introduces the possibility of recall bias, potentially impacting data reliability. Moreover, reproductive hormone assays were not conducted due to financial constraints, limiting the ability to explore the underlying mechanisms contributing to the increased CVD risk in postmenopausal women. Furthermore, 50 patients were excluded from the study due to incomplete data.

## Conclusion

Although most patients were undergoing therapeutic interventions, the prevalence of major CVD risk factors remained high among the studied women with T2DM. Close monitoring, targeted interventions, strict adherence to treatment regimens, and appropriate lifestyle modifications are essential to reducing the prevalence of these risk factors. The risk of CVD is significantly higher in postmenopausal women compared to those who have not yet experienced menopause. Further research on sex hormone levels is recommended to better understand the underlying mechanisms contributing to this increased risk. Key factors associated with elevated CVD risk in postmenopausal women with T2DM include high DBP, an

increased LDL/HDL ratio, and a longer duration since menopause. Beyond glycaemic management, it is crucial to closely monitor DBP, LDL, and HDL cholesterol levels in addition to other risk factors and implement timely therapeutic interventions, lifestyle changes to regulate blood pressure and optimize lipid profiles. Additionally, these contributing risk factors should be carefully considered when developing and validating CVD risk assessment tools tailored for women with T2DM in Sri Lanka.

## Abbreviations

|             |                                                           |
|-------------|-----------------------------------------------------------|
| BMI         | Body Mass Index                                           |
| CSTH        | Colombo South Teaching Hospital                           |
| CVD         | Cardiovascular disease (or Cardiovascular Diseases)       |
| DBP         | Diastolic Blood Pressure (or Diastolic BP)                |
| DM          | Diabetes Mellitus                                         |
| FBS         | Fasting Blood Sugar                                       |
| FRS         | Framingham Risk Score                                     |
| HDL         | High Density Lipoprotein                                  |
| LDL         | Low Density Lipoprotein                                   |
| LDL/HDL     | Low Density Lipoprotein to High Density Lipoprotein ratio |
| SBP         | Systolic blood pressure                                   |
| T-CHOL      | Total Cholesterol                                         |
| T. CHOL/HDL | Total Cholesterol to High Density Lipoprotein ratio       |
| T2DM        | Type 2 Diabetes Mellitus (or Type 2 Diabetic Women)       |
| WHR         | Waist-to-hip ratio                                        |

## Declarations

### Sources of funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

### Author Contribution

PKW, CW, ASF DSK and CG were involved in the design and conception of the study. PKW, CW, and ASF carried out the study and collected the data. They also entered the data into statistical software and cross-checked for accuracy. DSK and PKW analyzed the data, conducted statistical analysis, and, along with CG, contributed to data interpretation. The manuscript was written by PKW and DSK. All authors participated in reviewing, revising, and approving the final version of the manuscript.

### **Declaration of Ethics and Consent to Participate**

This study received ethical approval from the Ethical Review Committee of Colombo South Teaching Hospital, Kalumbila, Sri Lanka, (Application No:986, Approval date: 16.08.2021) and was conducted in accordance with the principles outlined in the Declaration of Helsinki. Written informed consent was obtained from all participants prior to enrollment.

### **Consent for publication**

Not applicable.

### **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.

### **Data availability**

The raw quantitative datasets used to support the findings of this study are deidentified participant data and are available from the corresponding author upon reasonable request.

### **Acknowledgements**

We sincerely appreciate the medical officers and staff of the Diabetes and Endocrinology Clinic at Colombo South Teaching Hospital for their invaluable support. The authors also extend their gratitude to all research participants for their time and cooperation throughout the study.

## **References**

1. Roth GA, Johnson C, Abajobir A, Abd-Allah F, Abera SF, Abyu G, et al. Global, Regional, and National Burden of Cardiovascular Diseases for 10 Causes, 1990 to 2015. *J Am Coll Cardiol*. 2017;70:1–25. <https://doi.org/10.1016/j.jacc.2017.04.052>.
2. Ministry of health -SriLanka. Status, determinants and interventions on cardiovascular disease & diabetes in Sri Lanka: a desk review of research 2000 – 2018. 2019.
3. Martín-Timón I. Type 2 diabetes and cardiovascular disease: Have all risk factors the same strength? *World J Diabetes*. 2014;5:444. <https://doi.org/10.4239/wjd.v5.i4.444>.
4. Arambewela MH, Somasundaram NP, Jayasekara HBPR, Kumbukage MP, Jayasena PMS, Chandrasekara CMPH, et al. Prevalence of Chronic Complications, Their Risk Factors, and the

- Cardiovascular Risk Factors among Patients with Type 2 Diabetes Attending the Diabetic Clinic at a Tertiary Care Hospital in Sri Lanka. *J Diabetes Res*. 2018;2018. <https://doi.org/10.1155/2018/4504287>.
5. World Heart Federation. Women and CVD - Facts and tips - World Heart Federation. 2017. <https://www.world-heart-federation.org/resources/women-cvd-facts-tips/>. Accessed 2 Apr 2021.
  6. Arnold AP, Cassis LA, Eghbali M, Reue K, Sandberg K. Sex hormones and sex chromosomes cause sex differences in the development of cardiovascular diseases. *Arteriosclerosis, Thrombosis, and Vascular Biology*. 2017;37:746–56. <https://doi.org/10.1161/ATVBAHA.116.307301>.
  7. Mauvais-Jarvis F. Is estradiol a biomarker of type 2 diabetes risk in postmenopausal women? *Diabetes*. 2017;66:568–70. <https://doi.org/10.2337/dbi16-0063>.
  8. Naftolin F, Friedenthal J, Nachtigall R, Nachtigall L. Cardiovascular health and the menopausal woman: The role of estrogen and when to begin and end hormone treatment [version 1; peer review: 3 approved]. *F1000Research*. 2019;8. <https://doi.org/10.12688/f1000research.15548.1>.
  9. Pardhe BD, Ghimire S, Shakya J, Pathak S, Shakya S, Bhetwal A, et al. Elevated Cardiovascular Risks among Postmenopausal Women: A Community Based Case Control Study from Nepal. *Biochem Res Int*. 2017;2017. <https://doi.org/10.1155/2017/3824903>.
  10. Grandi SM, Filion KB, Yoon S, Ayele HT, Doyle CM, Hutcheon JA, et al. Cardiovascular Disease-Related Morbidity and Mortality in Women with a History of Pregnancy Complications: Systematic Review and Meta-Analysis. *Circulation*. 2019;139:1069–79. <https://doi.org/10.1161/CIRCULATIONAHA.118.036748>.
  11. Shufelt CL, Bairey Merz CN. Contraceptive Hormone Use and Cardiovascular Disease. *Journal of the American College of Cardiology*. 2009;53:221–31. <https://doi.org/10.1016/j.jacc.2008.09.042>.
  12. Okoth K, Chandan JS, Marshall T, Thangaratnam S, Thomas GN, Nirantharakumar K, et al. Association between the reproductive health of young women and cardiovascular disease in later life: Umbrella review. *The BMJ*. 2020;371. <https://doi.org/10.1136/bmj.m3502>.
  13. Tobias DK, Stuart JJ, Li S, Chavarro J, Rimm EB, Rich-Edwards J, et al. Association of history of gestational diabetes with long-term cardiovascular disease risk in a large prospective cohort of US women. *JAMA Intern Med*. 2017;177:1735–42. <https://doi.org/10.1001/jamainternmed.2017.2790>.
  14. Selvarajah S, Kaur G, Haniff J, Cheong KC, Hiong TG, Van Der Graaf Y, et al. Comparison of the Framingham Risk Score, SCORE and WHO/ISH cardiovascular risk prediction models in an Asian population. *Int J Cardiol*. 2014;176:211–8. <https://doi.org/10.1016/j.ijcard.2014.07.066>.
  15. Jahangiry L, Farhangi MA, Rezaei F. Framingham risk score for estimation of 10-years of cardiovascular diseases risk in patients with metabolic syndrome. *J Health Popul Nutr*. 2017;36:1–6. <https://doi.org/10.1186/s41043-017-0114-0>.
  16. Al-Lawati JA, Barakat MN, Al-Lawati NA, Al-Maskari MY, Elsayed MK, Mikhailidis DP, et al. Cardiovascular risk assessment in diabetes mellitus: Comparison of the general framingham risk profile versus the World Health Organization/ International Society of Hypertension risk prediction charts in Arabs - Clinical implications. *Angiology*. 2013;64:336–42. <https://doi.org/10.1177/0003319712458349>.

17. DAWBER TR, MOORE FE, MANN G V. Coronary heart disease in the Framingham study. *Am J Public Health Nations Health*. 1957;47:4–24. [https://doi.org/10.2105/ajph.47.4\\_pt\\_2.4](https://doi.org/10.2105/ajph.47.4_pt_2.4).
18. Vogel B, Acevedo M, Appelman Y, Bairey Merz CN, Chieffo A, Figtree GA, et al. The Lancet women and cardiovascular disease Commission: reducing the global burden by 2030. *The Lancet*. 2021;397:2385–438. [https://doi.org/10.1016/S0140-6736\(21\)00684-X](https://doi.org/10.1016/S0140-6736(21)00684-X).
19. Section 4: Guide to Physical Measurements (Step 2) WHO STEPS Surveillance Section 4: Guide to Physical Measurements (Step 2) Overview.
20. Guidelines for the management of dyslipidaemia in patients with diabetes mellitus Quick reference guide. 2006.
21. World health organization. Obesity and overweight. 2020. <https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight>. Accessed 27 Apr 2021.
22. Waist Circumference and Waist-Hip Ratio: Report of a WHO Expert Consultation. 2008.
23. Unger T, Borghi C, Charchar F, Khan NA, Poulter NR, Prabhakaran D, et al. 2020 International Society of Hypertension Global Hypertension Practice Guidelines. *Hypertension*. 2020;75:1334–57. <https://doi.org/10.1161/HYPERTENSIONAHA.120.15026>.
24. Canadian Cardiovascular society. Framingham's risk score worksheet. 2017. [https://ccs.ca/app/uploads/2020/12/FRS\\_eng\\_2017\\_fnl\\_greyscale.pdf](https://ccs.ca/app/uploads/2020/12/FRS_eng_2017_fnl_greyscale.pdf). Accessed 22 Mar 2021.
25. Gamlath L, Nandasena S, Silva P De, Morrell S, Linhart C, Lin S, et al. Community intervention for cardiovascular disease risk factors in Kalutara, Sri Lanka. *BMC Cardiovasc Disord*. 2020;20. <https://doi.org/10.1186/s12872-020-01427-y>.
26. Wijewardene K, Mohideen M, Mendis S, Fernando D, Kulathilaka T, Weerasekara D, et al. Prevalence of hypertension, diabetes and obesity: baseline findings of a population based survey in four provinces in Sri Lanka. *Ceylon Medical Journal*. 2010;50:62. <https://doi.org/10.4038/cmj.v50i2.1571>.
27. Yang L, Lin L, Kartsonaki C, Guo Y, Chen Y, Bian Z, et al. Menopause characteristics, total reproductive years, and risk of cardiovascular disease among Chinese women. *Circ Cardiovasc Qual Outcomes*. 2017;10. <https://doi.org/10.1161/CIRCOUTCOMES.117.004235>.
28. Riise HKR, Sulo G, Tell GS, Igland J, Nygård O, Iversen AC, et al. Association between gestational hypertension and risk of cardiovascular disease among 617 589 Norwegian women. *J Am Heart Assoc*. 2018;7. <https://doi.org/10.1161/JAHA.117.008337>.
29. Peters SAE, Van Der Schouw YT, Wood AM, Sweeting MJ, Moons KGM, Weiderpass E, et al. Parity, breastfeeding and risk of coronary heart disease: A pan-European case-cohort study. *Eur J Prev Cardiol*. 2016;23:1755–65. <https://doi.org/10.1177/2047487316658571>.
30. Zhou H, Zhang C, Ni J, Han X. Prevalence of cardiovascular risk factors in non-menopausal and postmenopausal inpatients with type 2 diabetes mellitus in China. *BMC Endocr Disord*. 2019;19:1–9. <https://doi.org/10.1186/s12902-019-0427-7>.

## Footnotes

[1] LDL – Low Density Lipoprotein, HDL – High Density Lipoprotein, BMI – Body Mass Index, WHR – Waist to Hip Ratio.

[2] DM – Diabetes Mellitus, CVD- Cardiovascular Diseases, BMI – Body Mass Index, WHR – Waist to Hip Ratio, FBS – Fasting Blood Sugar, LDL – Low Density Lipoprotein, HDL- High Density Lipoproteins, T-CHOL – Total Cholesterol

[3] FBS- Fasting Blood Sugar, LDL – Low Density Lipoprotein, T. CHOL/HDL – Total Cholesterol to High Density Lipoprotein ratio, LDL/HDL – Low Density Lipoprotein to High Density Lipoprotein ratio, DBP – Diastolic Blood Pressure, DM – Diabetes Mellitus.