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Original Article

# Pulse wave analysed cardiovascular parameters in young first degree relatives of type 2 diabetics- a cross-sectional study

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ABSTRACT

*Background:* First degree relatives (FDR) of type 2 diabetic (T2D) are predisposed for type 2 diabetes mellitus (T2DM) which accelerates cardiovascular ageing. Pulse wave analysis (PWA) gives non-invasive measurement of central haemodynamics like central blood pressure (cBP), cardiac output(CO), stroke work (SW) and vascular stiffness like pulse wave velocity (PWV) and augmentation index at heart rate 75 (AIx@75).
*Objective:* To study PWA derived cardiovascular parameters in FDRs of type 2 diabetic (T2D) as compared to controls.
*Materials and methods:* We enrolled 117 FDRs of T2D and 117 matched controls for a cross-sectional study. We performed pulse wave analysis (PWA) using Mobil-o-Graph (IEM, Germany) by oscillometric method to derive cardiovascular parameters which were compared and correlated for significance. P value less than 0.05 was considered statistically significant.
*Results:* Gender, age, height, weight, BMI, physical activity were comparable between groups. FDRs of T2D had significantly higher blood pressure (brachial-systolic 125 vs 118, diastolic 80 vs 77, mean 100 vs 96 mm of Hg and central- systolic 113 vs 105, diastolic 82 vs 79, pulse pressure 31 vs 28 mm of Hg), SW(98 vs 90 g m/bt), rate pressure product (RPP- 113 vs 107), PWV (5.14 vs 4.89 m/s), AIx@75 (30 vs 27) than control. Dependant variables correlated with brachial BP more than age or anthropometric variables.
*Result:* didnot differ by maternal or paternal inheritance in case group.
*Conclusions:* Young, sedentary, non-obese FDRs of T2D have adverse cardiovascular profile which is suggested to worsen before or with onset of T2DM and definitely need attention for life style modification as primary prevention.


## 1. Introduction

Rise of type 2 diabetes mellitus (T2DM) with worrying future trend for world and India[1] is known so as the concept of early onset of diabetes.[2] Positive family history is most significant and independent predisposing factor for T2DM.[3] It is thought to be, sometimes, a disease of vascular ageing with hyperglycaemia as late manifestation.[4] Cardiovascular ageing is early and accelerated once T2DM ensues,[5] but whether is it a risk for the same in young first degree relatives (FDRs) of type 2 diabetics (T2D), remains a question. It more so probable if FDR of T2D is sedentary,[2] living stressful life. It can be measured non-invasively by pulse wave analysis[6] under headings of haemodynamic parameters like central blood pressure (cBP), cardiac output (CO), stroke work (SW), rate pressure product (RPP) and vascular stiffness parameters like augmentation pressure (AP), pulse wave velocity (PWV) and augmentation index (AIx). We tested the hypothesis of early cardiovascular ageing in young FDRs of type 2 diabetics as compared to matched controls.

## 2. Materials and methods

### 2.1. Study design and subjects

We conducted a community based observational study at clinical research laboratory of Physiology department of a government medical college attached to tertiary care teaching government hospital from 18th June 2015 to 25rd April 2016. Prior approval for the study was taken from institutional review board and each participant gave written informed consent. We enrolled, using convenience sampling method, from our institute total 482 apparently healthy subjects with known parental history of type 2

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diabetes and hypertension. After scrutiny we finally had 117 subjects as first degree relatives (FDR) of type 2 diabetic taken as case group. We excluded subjects with family history of hypertension from current study. Of remaining participants, we set to make a control group of 117 subjects matched to case group by age, gender, BMI and physical activity, but with negative family history of type 2 diabetes [Fig. 1].

### 2.2. Inclusion and exclusion criteria

We included FDRs type 2 diabetics(T2D), aged 15 to 35 years, of either sex, not known for any disease, not taking any medical treatment(including anti-diabetic medication), living sedentary life style, ready for written consent. We excluded subjects known to have type 2 diabetes, aged more than 35 years or less than 15 years, having hypertension, any acute or chronic cardiovascular diseases, denying written consent, having any disease or drug history, current or ex-smokers or tobacco chewers, trained athletes, subjects using of any alternative system of medicines/ life style managements like Yoga and mediation. We excluded one subject from analysis after pulse wave recording due to irregular pulse wave rhythm. Criteria for control group were similar as above except absence family history of type 2 diabetes.

### 2.3. Initial assessment and definitions

We personally interviewed all subjects before enrolment. It was in the form of questionnaires including general features, demographic characteristics, height, weight, disease history, drug history, life style intervention used, intake of tea, coffee, alcohol or meal, sleep history and family history of T2DM and hypertension.

Diabetes mellitus was defined as per the American Diabetes Association criteria 2014.[7]

First degree relative (FDR) of T2D was defined as subject having either a parent or a grandparent having known type 2 diabetes mellitus.

Systolic blood pressure less than 140 mm of Hg and diastolic blood pressure less than 90 mm of Hg were defined as controlled blood pressure.

### 2.4. Instrument used[6–10]

We used portable, PC attached, calibrated and validated instrument Mobil-o-Graph(IEM Gmbh, Stolberg, Germany) owned by Physiology department to record brachial pulse wave. It performs pulse wave analysis based on Oscillometric method. Arterial pulsation generates the pressure oscillations which are transmitted to blood pressure cuff and measured by transducer to be fed into microprocessor. Computerized software records pulse wave from brachial artery and by a transfer factor derives central aortic pulse wave. It further undergoes point based and area based analysis by computer to derive various cardiovascular parameters.

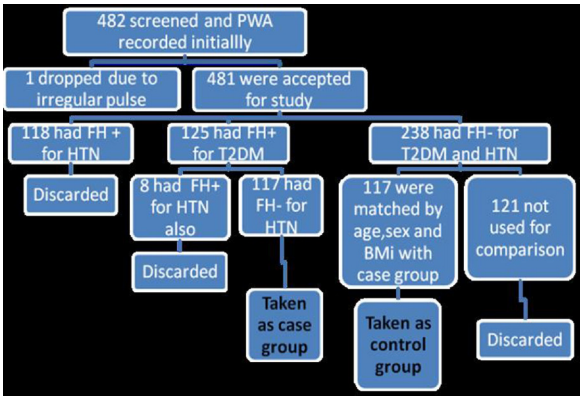


**Fig. 1.** Study subjects selection-flow chart.

### 2.5. Measurement protocol

A BP cuff of appropriate size was chosen based on mid arm circumference(Small, Medium or Large) and applied to left arm using standard protocol. All readings were taken after 10 min of rest, in post absorptive phase with subjects avoiding smoking or alcohol for 12 h before the test, in a calm room avoiding external influences or arm movement.

### 2.6. Parameters measured

1) Heart rate (HR), body mass index (BMI), body surface area (BSA)
2)Brachial blood pressure (bBP)-systolic (bSBP), diastolic (bDBP), pulse (bPP)and mean (bMBP)
3) Central blood pressure (cBP) – systolic (cSBP), diastolic (cDBP), pulse (cPP)
4) Central hemodynamics- cardiac output (CO), cardiac index (CI), systemic vascular resistance (SVR)
5) Arterial stiffness- augmentation pressure (AP), augmentation index at heart rate 75 per minute (AIx@75), reflection magnitude percentage (Ref%), pulse wave velocity(PWV)

### 2.7. Parameters derived

1) Rate pressure product (RPP)[11] – (heart rate per minute) × ( systolic blood pressure) × $10^{-2}$
2) Stroke volume (SV) – cardiac output/heart rate
3) Stroke volume index (SVI) – stroke volume/body surface area
4) Stroke work (SW)[12]- (pulse pressure) × (stroke volume) × 0.0144
5) Total arterial stiffness (TAS)[13]- pulse pressure/stroke volume

### 2.8. Statistical analysis

Sample size was calculated by Raosoft software (Raosoft, Inc. free online software, Seattle, WA, USA). To have 95% confidence level and 5% precision, a sample size of 138 (Considering either parent diabetic for each subject, size is halved to 62) for population of the city 6 lakhs with 8.7% prevalence of type 2 diabetes mellitus in Asian region[14] was adequate. The data was transferred on Excel spreadsheet and descriptive analysis was expressed as mean ± standard deviation until specifically indicated. All calculations were done by Graph Pad in Stat 3 software (demo version free software of GraphPad Software, Inc. California, USA) and MedCalc Statistical Software version 16.4.3 (MedCalc Software bvba, Ostend, Belgium; https://www.medcalc.org; 2016). We calculated the statistical significance of differences in mean distribution of various parameters between various groups by Mann-Whitney test or unpaired student *t*-test for quantitative data and by Normality test for qualitative data. Spearman's correlation test was used for correlation between parameters – parametric or nonparametric. Statistical significance level was set at $p < 0.05$.

## 3. Results

Case and control group were comparable in age (mean 22 years) and gender (68 males,49 females in each), with matched height (mean 163 vs 162 cm),weight (mean 58.86 vs 58.38 kg), BMI (Mean 22.13 vs 22.14 kg/m$^2$),BSA (mean 1.62 vs 1.61 m$^2$)and physical

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