RESEARCH ARTICLE

Comparative study of ankle brachial pressure index and blood sugar profile among offspring of diabetic and non-diabetic parents in early detection of peripheral arterial disease

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ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) is a complex disorder which is caused by a composite combination of genetic, epigenetic, and environmental factors. One of the most contributing quantitative risk factors is family history. The prevalence of peripheral arterial disease (PAD) in T2DM ranges from 20% to 30% and the lifetime risk of developing diabetes is up to 40% if either of parents is type 2 diabetic. Aim and Objectives: The aim of the study was to know whether non-diabetic offsprings of diabetic parents having chances of becoming diabetic and to have PAD in future part of life. Material and Methods: Taking all inclusion and exclusion criteria into consideration, 50 offsprings of diagnosed diabetic parents (>5 years) were taken as cases, and 50 healthy age-matched offsprings were taken from non-diabetic parents as controls. A thorough physical and systemic examination were done. After getting informed written consent, anthropometric measurements, FBS, PPBS, HbA1c, were measured. By taking ankle systolic blood pressure (SBP) and brachial SBP, ankle-brachial pressure index (ABPI) was calculated using a hand held vascular Doppler. Statistical analysis was done by Student’s t-test in SPSS software. Results: The mean HbA1c (%) level for controls was 5.68 ± 0.35 and for cases was 5.85 ± 0.44 with a P-value of 0.035 (significant). Similarly mean values for ankle SBP (mm Hg) were 148.4 ± 17.33 in controls and 159.8 ± 23.66 in cases with a P-value 0.0071 (significant). About 32% of controls and 50% of cases showed a non-compressible ABPI (ncABPI) arteries of >1.3, whereas only 2% of cases showed a typical ABPI of PAD, that is, <0.9. Conclusion: HbA1c being slightly higher in cases as compared to controls, points toward some ongoing dysregulation of blood glucose levels. With a ncABPI ratio being more in cases than in controls, our study showed that offsprings of diabetic parents are at more risk to develop atherosclerotic related complications such as PAD and CVD in future.

KEY WORDS: Type 2 Diabetes; Peripheral Arterial Disease; Ankle-Brachial Pressure Index; HbA1c; Atherosclerosis; Monckeberg’s Arteriosclerosis

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a complex disorder which is caused by a composite combination of genetic, epigenetic and environmental factors. The prevalence of the disease is progressively on the rise, 171 million people had diabetes in the year 2000 and it is estimated that number will rise to 366 million by 2030.\(^{1}\) One of the most contributing quantitative risk factors is family history. Family history of T2DM is seen to have significant role in the acquisition of diabetes in the later generations and acts as one of the major risk factors as mentioned by Indian Diabetic Risk Score, for screening of non-diabetic individuals. Several previous studies stated that first degree relatives of T2DM patients are at high risk for T2DM, as they are likely to share genetic predisposition and
have similar lifestyle. However, among T2DM offsprings, self-perception and recognition that they are at high risk for diabetes compared to general population are only 63.5%.[2]

The prevalence of peripheral arterial disease (PAD) in T2DM ranges from 20% to 30% and the lifetime risk of developing diabetes is up to 40% if either of parents is type 2 diabetic.[3] A follow-up study stated that, sometimes blood glucose may appear normal but 20% of patients with PAD can develop diabetes in later years.[4] Hence, majority of patients are asymptomatic and go undiagnosed. The American Diabetic Association has estimated that 40–50% of the diabetic related amputations are preventable.[5] The diagnostic test most used to check such asymptomatic population is the ankle-brachial pressure index (ABPI). ABPI is simple, non-invasive, rapid test for screening and diagnosing with 92.85% sensitivity and 100% specificity.[4] Therefore by identifying these offsprings with subclinical disease or those with parental history and by instituting preventive measures, it may be possible to avoid acute limb-threatening ischemic complications.

No comprehensive study is available so far on early detection of PAD in non-diabetic offsprings of diabetic parents using ABPI. Hence, current study is done to assess and compare; lipid profile and vascular changes which indirectly point towards insidious onset of atherosclerosis among offsprings of diabetic and non-diabetic parents. If any such indirect genetic correlation among offsprings of diabetic parents is present, then it will be helpful in early detection of T2DM and PAD in future.

MATERIAL AND METHODS

This study was conducted in the department of Physiology, KIMS Hubballi with the assistance of laboratory setup of the department of Biochemistry, KIMS, Hubballi. Ethical approval was obtained from the ethical committee of KIMS, Hubballi on November 24, 2018.

Study Design

It is a cross-sectional study in which statistical analysis was done using “SPSS Software” with the help of Biostatistician, KIMS Hubballi.

Source of Data

Case papers of patients visiting KIMS General medicine department were examined. Confirmed, diagnosed, and regular follow-up patients of T2DM were noted down. Their offsprings who matched the inclusion and exclusion criteria were taken as cases (50). Similarly, age-matched healthy individuals’ offsprings were taken as controls (50). A predesigned questionnaire was filled by me which included details such as name, age, sex, family history of diabetes, history of smoking, alcohol consumption, tobacco chewing, and history to rule out all exclusion criteria.

Inclusion Criteria

The following criteria were included in the study:

- Age group: 40–55 years
- Gender: Both males and females were included
- Offsprings of known T2DM patients visiting KIMS hospital Hubballi were taken as cases (whose either/both parents were clinically diagnosed with T2DM – duration >5 years).
- Age matched offsprings of Non-diabetic parents were taken as controls.

Exclusion Criteria

Persons already diagnosed with/any previous history of/who are on treatment for:

- Diabetes, hypertension, and thyroid problems
- Below 40 years or above 55 years of age
- Stroke, ischemic heart disease
- Smoking, Tobacco chewing, Alcohol consumption, Hematological disorders
- Deep vein thrombosis, leg ulcers, limb deformities, Peripheral vascular disease, Claudication, rest/nocturnal pain, loss of hair over limb, cold feet, Varicose veins, Buerger’s disease, and thoracic outlet syndrome
- In females - Polycystic ovarian syndrome, consumption of oral contraceptives
- Unstable (hypotensive and respiratory distress) and unable to undergo the tests.

After selecting the cases and controls, appointment was scheduled in prior and they were requested to do an overnight fasting prior to the day of the test to get fasting blood sample for blood sugar and ABPI analysis. Samples were collected in morning session around 8 am. PPBS was done after 2 hours of having adequate breakfast. Detailed physical examination was done. After explaining the test procedure in their own vernacular language, written consent form was obtained to participate in the study.

1) Anthropometric measurements were taken and BMI, WHR were calculated.
2) Blood samples were collected.

Normal values for HbA1c as defined by American diabetes association (ADA): Normal – <5.7% prediabetes – 5.7–6.4% diabetes – 6.5% or higher.

3) ABPI measurement: Controls and cases were instructed to lie down for 10 min comfortably and resting blood pressure was recorded. After checking BP, brachial pulse was palpated in the right arm. At the site where pulse was felt, conducting gel was applied and Doppler signal was obtained by placing the probe at a 60° angle towards the patient’s head.[6] BP cuff was inflated rapidly to 20–30 mmHg above the point of cessation.
of brachial-artery flow, then slowly cuff was deflated in order to note the brachial systolic blood pressure (SBP) (the pressure flow sound which is first heard over Doppler while deflating). Gel applied on the skin was wiped with cotton. After measuring the systolic pressure in arm, cuff was placed 2 fingers above the right ankle. To measure ankle SBP, posterior tibial artery was chosen because dorsalis pedis artery pulse might be absent in up to 12% of population.[3] The anatomical landmark to feel for the posterior tibial artery pulse is slightly posterior to medial malleolus. Once pulse was felt, conducting gel was applied and Doppler probe was placed on the artery site that induced best Doppler signal. Once again BP cuff was inflated 20–30 mmHg above the level at which flow ceases, then cuff was slowly deflated and ankle SBP was noted. With the obtained values ABPI was calculated using the formula:

\[
ABPI = \frac{\text{Ankle systolic blood pressure (mm Hg)}}{\text{Brachial systolic blood pressure (mm Hg)}}
\] (1)

**Standard ABPI Values**

Normal ABPI ranges from 0.91 to 1.30. Reading above 1.30 is usually suggestive of partial incompressible arteries which are likely to be due to medial arterial calcification also called as Monckeberg’s arteriosclerosis. Mild to moderate PAD usually produces an ABPI in the range of 0.41–0.90. Below 0.40 suggests the presence of severe PAD.[3]

**RESULTS**

Mean HbA1c value was higher in cases as compared to controls. The P-value (0.035) for the following parameter showed a significant difference. The P-value (0.08) of Brachial SBP found to be not significant whereas P-value (0.0071) of Ankle SBP showed very highly significant difference. Controls having an ABPI <0.9 were 0% (None among 50). Controls within a range of 0.9–1.3 were 68% (34 people). ABPI of values >1.3 were 32% (16 people). Cases having an ABPI <0.9 were 2% (1 person out of 50). ABPI within a range of 0.9–1.3 were 48% (24 people). ABPI of values >1.3 were 50% (25 people) [Table 1].

**DISCUSSION**

Our present study is a cross-sectional study which showed HbA1c and ankle SBP as significant parameters when compared between non-diabetic offsprings of T2D parents and non-diabetic offsprings of non-diabetic parents. Hence, discussion for these parameters will be made in following headings.

**Association of HbA1c with Family History of T2D and PAD**

In the present study, mean HbA1c (%) level for controls was 5.68 ± 0.35 and for cases was 5.85 ± 0.44 with a P-value of 0.035 (significant). As per the new guidelines proposed by ADA, the mean HbA1c values of our cases fall into “prediabetics” category.[5] In our study, we found that HbA1c was slightly higher in case of non-diabetic offsprings of diabetic parents as compared to offsprings of non-diabetic parents. This suggests there must be a genetic component being carried to these non-diabetic children of diabetic parents. However, with these levels of HbA1c we could not find a linear correlation with PAD probably because of the reason that, subjects chosen for our study were relatively healthy. However, the risk of family history as a predominant risk factor and prediabetic range of their HbA1c cannot be ignored. Glycation increases the chemical binding of lipoproteins to vessel wall proteins, promoting sequestration, free radical damage, and hence inducing inflammation which all further lead to the onset of atherosclerosis followed by PAD as per Akalu and Birhan et al. (2020). [6] Thus, offsprings of diabetic parents can be advised about future risk perceptions and life style modifications to prevent further possible complications.

Wheeler et al. (2017) stated in their genetic study that, every 1% increase in HbA1c in individuals without T2D but with parental history was associated with a more than 2 fold increase in risk of developing future T2D and a 20–50% increase in risk of vascular complications. Likewise Wheeler et al. (2006) showed in their study that, individuals with poor glucose control (HbA1c >7.5%) were more than 5 times as likely to have PAD as compared to those with good glycemic control (HbA1c <6%).[9] However, a 14-year follow-up study done by Shukla et al. did not find a fix HbA1c threshold for microvascular outcomes before or after adjusting the covariates.

A study conducted by Shukla et al. (2018) showed 63.8% of T2D cases had asymptomatic PAD with a mean HbA1c of 7.48 ± 1.16.[10] Similarly, in a study conducted by Patel and Jani (2013) for the prediction of PAD in diabetics and non-diabetics, the mean HbA1c in PAD subjects was 9.23 and in Non-PAD was 6.43 with a P < 0.001. Their study showed a highly significant correlation between HbA1c levels and PAD.[10]

Rabia and Khoo (2007) conducted a study on 100 cases of T2D with diagnostic duration and treatment of more than 10 years. By including other risk factors such as smoking, hypertension, they got a mean HbA1c of 8.38 ± 8.12. In spite of taking above mentioned risk factors into consideration in clinically diagnosed T2D cases, they did not find any significant association of HbA1c levels and PAD.[5]
### ABPI and PAD

In the present study, we got a significant difference of ankle SBP (mm Hg) among controls and cases with a mean of 148.4 ± 17.33 in controls and 159.8 ± 23.66 in cases (with a *P*-value 0.0071). ABPI ratio in our study was 1.25 ± 0.112 for controls and 1.308 ± 0.188 (*P*-value = 0.096 = not significant) for cases.

As per the genetic review article by Kullo and Leeper (2015), predisposition to PAD may be influenced by various genetic factors. They have mentioned about association of 3 single nucleotide polymorphisms covariate interactions (i.e., ADRB2 Gly 16 – lipoprotein a and SLC4A5 – diabetes) were responsible for a positive ABPI finding of PAD associated with T2D. Except genetic theories, no studies have been postulated as far to evaluate early detection of PAD by an indirect offspring-parent approach. In our study, the typical ABPI prevalence indicative of PAD, that is, <0.9 was 0 in controls and 2% in cases. Similarly, ABPI between 0.9 and 1.3 (i.e., normal range) was 68% in controls and 48% in cases. Finally, ABPI >1.3 (Monckeberg’s arteriosclerosis) was 32% in controls and 50% in cases.

According to studies conducted by Singh et al. (2017) and Patel and Jani (2013), a non-compressible ABPI (ncABPI) of >1.3 is histologically associated with medial arterial calcification (Monckeberg's calcific sclerosis). When used as a screening tool, the presence of ncABPI can mask or cofound the detection of PAD. Many studies also state, a ncABPI of >1.3 is associated with increased cardiovascular events and mortality when compared to the over-all population of patients with PAD.

Monckeberg’s arteriosclerosis is a form of vascular hardening where calcium deposits are found in the tunica media of arteries. Although this condition occurs as an age related degenerative process, it has been proposed that it is a continuum of atherosclerotic disease as the majority of atherogenic plaques always contain some calcium deposits. The prevalence of Monckeberg’s arteriosclerosis increases with age and is more frequent and early in diabetics. Typically, it is not associated with symptoms unless complicated by atherosclerosis and other diseases.

Many of the literatures state that, atherosclerosis may be the result of various factors such as impaired lipid metabolism, increased cholesterol in diet, decreased physical activity, smoking, hypertension, diabetes, whereas arteriosclerosis is a “genetic trait” that cannot be changed. Pursuing this into our knowledge, 32% of controls (offsprings of non-diabetic parents) and 50% of cases (offsprings of diabetic parents) showed a ncABPI of >1.3 in our study. This shows that, offsprings of diabetic parents are at 18% more risk for an accelerated development of atherosclerosis, PAD or CVD in future. On the other hand, ABPI showing typical diagnosis of PAD (i.e., <0.9) was only 2% among cases. Although it is not statistically significant in identifying any genetic component involved in the inheritance of PAD along with diabetic trait, we recommend further genetic studies and other advanced angioinvasive techniques to rule out the possibilities completely.

### PAD

Tyagi et al. (2017) in their study included 100 T2D patients including history of smoking, alcohol, signs and symptoms of PAD. The prevalence for PAD obtained was 40%. Similarly study conducted by Shukla et al. (2018) on 200 T2D patients showed a prevalence of 36%. The mean FBS and PPBS in their study for PAD subjects was 187.90 ± 100.64 and 280 ± 121.11, respectively. Rabia and Khoo (2007) conducted a study on T2D cases which included history of smoking, ulcerated foot lesions, gangrene and the prevalence for PAD they got was 16%. Patel and Jani (2013) got a prevalence of 73% in diabetics and 30% in non-diabetics. The mean FBS in PAD subjects was 172.87 ± 64.26 while for non-PAD subjects were 119.55 ± 43.05. In case of PPBS mean for PAD subjects was 122.8 ± 14.05 and in non-PAD subjects 119.55 ± 43.05.

### Table 1: Mean values, *P*-values of corresponding parameters and their significance

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Controls (Mean±SD)</th>
<th>Cases (Mean±SD)</th>
<th><em>P</em>-value</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>46.1±3.17</td>
<td>45.12±4.59</td>
<td>0.21</td>
<td>NS</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.2±3.5</td>
<td>24.38±2.85</td>
<td>0.161</td>
<td>NS</td>
</tr>
<tr>
<td>WHR</td>
<td>0.91±0.10</td>
<td>0.88±0.06</td>
<td>0.145</td>
<td>NS</td>
</tr>
<tr>
<td>FBS (mg/dl)</td>
<td>78.86±13.92</td>
<td>81.9±0.67</td>
<td>0.125</td>
<td>NS</td>
</tr>
<tr>
<td>PPBS (mg/dl)</td>
<td>110.5±11.92</td>
<td>115±16.65</td>
<td>0.123</td>
<td>NS</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>5.68±0.35</td>
<td>5.85±0.44</td>
<td>0.035</td>
<td>S</td>
</tr>
<tr>
<td>Systolic BBP (mm Hg)</td>
<td>118.2±11.89</td>
<td>122.8±14.05</td>
<td>0.080</td>
<td>NS</td>
</tr>
<tr>
<td>Systolic ABP (mm Hg)</td>
<td>148.4±17.33</td>
<td>159.8±23.66</td>
<td>0.007</td>
<td>VHS</td>
</tr>
<tr>
<td>ABPI</td>
<td>1.25±0.112</td>
<td>1.308±0.188</td>
<td>0.096</td>
<td>NS</td>
</tr>
</tbody>
</table>

S: Significant, VHS: Very highly significant, NS: Not significant, SBP: Systolic blood pressure, SD: Standard deviation, ABPI: ankle-brachial pressure index.

*P*-values of corresponding parameters and their significance

### References

- Kullo and Leeper (2015)
- Singh et al. (2017)
- Patel and Jani (2013)
- Rabia and Khoo (2007)
- Shukla et al. (2018)
- Tyagi et al. (2017)
Major noticeable findings in above mentioned studies are; first - many of the researchers did not exclude risk factors like smoking (as smoking itself is a potent trigger for occurrence of PAD) or already appeared signs and symptoms of PAD. Second - subjects included in the studies had clinically diagnosed T2DM with on-treatment duration of minimum >5-8 years. Third - the mean FBS and PPBS levels were constantly elevated for a prolonged period of time, whereas in our study, subjects chosen were relatively healthy with strict inclusion and exclusion criteria. The mean FBS (mg/dl) was 78.86 ± 13.92 for controls and 81.9 ± 0.067 for cases, likewise mean PPBS (mg/dl) was 110.5 ± 11.92 for controls and 115 ± 16.65 for cases. This shows that as long as FBS and PPBS remain normal, ABPI is not going to be altered significantly.

**Limitations**

1. The present study suffers from a limitation in terms of sample size, making it difficult to extract significant prevalence values for early detection of PAD.
2. Study needs plasma insulin levels of cases that would have helped to come to conclusion in a definite way.

**Further Recommendations**

Offsprings of diabetic parents have got slightly higher mean HbA1c levels than controls in the study. Hence, it is recommended to have HbA1c checkup once in 3 months to prevent further complications. ABPI as an indicator of asymptomatic PAD has certain limitations, thus to rule out early vascular anatomy and pathological changes, it should be conjoined with other investigations such as duplex ultrasonography, angiography, or (MDCT) multi detector computer tomography.

The increasing drive toward primary prevention of diabetes, the information from current study could be a powerful motivation to adult family members of people with T2D as strong family history. A reminder of knowledge and attitudes towards risk factors of both affected and their relatives, who are in a progressive path towards disorder can throw light on some prevention measures such as - food style modifications, regular physical activity, and periodic monitoring of health check-ups.

**CONCLUSION**

It is a cross-sectional comparative study conducted among 50 non-diabetic offsprings of diabetic parents who are the patients drawn from KIMS hospital Hubballi and 50 Non-diabetic offsprings of non-diabetic parents from KIMS medical college Hubballi. The parameters measured in this study were; BMI, WHR, FBS, PPBS, HbA1c, Brachial SBP, Ankle SBP, and ABPI. Parameters which showed significant difference were HbA1c and Ankle SBP.

The mean HbA1c (%) was higher in cases as compared to controls. This could be due to relative insulin deficiency and glucose transporter receptors’ resistance. Similarly mean value for ankle SBP (mm Hg) was higher in cases as compared to controls. This could be due to mild atherosclerotic changes in the blood vessels of lower limbs. However, there is no significant difference in the brachial SBP. About 32% of controls (offsprings of Non-diabetic parents) and 50% of cases (offsprings of diabetic parents) showed a nCA/ABI of >1.3 in our study depicting offsprings of diabetic parents are at 18% more risk to develop atherosclerotic related complications like PAD and CVD in future. Whereas, only 2% of cases showed a typical ABI of PAD, that is, <0.9, which is negligible to elicit genetic component as risk factor for PAD.

**REFERENCES**

12. Singh GD, Armstrong EJ, Waldo SW, Alvandi B, Brinza E, Hildebrand J, et al. Non-compressible ABIs are associated with an increased risk of major amputation and major adverse


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