Pulse Oximetry As The Potential Screening Tool For Lower Extremity Arterial Disease In Asymptomatic Patients With Diabetes Mellitus

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Abstract:

Background: Lower extremity arterial disease (LEAD) is common and under Diagnosed in patients with Diabetes Mellitus (DM) Risk persists even when LEAD is Subclinical. It is an important socio-economical and healthcare problem, due to its High incidence of morbidity, disability and mortality and its related cardiovascular events. Early detection of LEAD, before the onset of symptoms in patient with DM, is desirable and can lead to tighter, better control of risk factors for arterial disease. Present study is an effort to compare for the accuracy of Pulse Oximetry, the Ankle-Brachial index (ABI) and the combination of the two to diagnose LEAD in Asymptomatic type 2 DM patients. Methods: Fifty type 2 DM patients who had no symptoms of LEAD attending OPD and IPD in Dr.B.R.Ambedkar medical college during recent 2 years were enrolled. Exclusions were age <40 years, known LEAD, or typical symptoms of LEAD. All patients had (1) ABI measurement and considered abnormal < 0.9 (2) pulse oximetry to measure SaO₂ of their index fingers and big toes in the supine position and SaO₂ of the toes was considered abnormal if the SaO₂ was more than 2% lower from the finger. The combination was considered positive if either the ABI or pulse oximetry was positive for LEAD and negative if both were negative. And (3) Doppler waveform analysis of the lower extremity arteries used as standard comparison for above tests and defined LEAD as monophasic waveforms. Results: Of our 50 patients (100 legs examined), 31 (31%) had LEAD. Pulse Oximetry has a Sensitivity of 74.14%, Specificity of 97.10%, and Positive predictive value of 92% and Negative predictive value of 89.3%. ABI has a Sensitivity of 60.60%, Specificity of 97.12%, and Positive predictive value of 90.9% and Negative predictive value of 87.9%. Combination has a Sensitivity of 87%,
Specificity of 94.20%, and Positive predictive value of 87% and Negative predictive value of 94.20%. **Conclusion:** Pulse oximetry of the toes seems to be simple and as accurate as ABI to Screen for LEAD in patients with Type 2 Diabetes. Combination of the two tests increases sensitivity.

**Key words:** Ankle-Brachial index (ABI); Diabetes Mellitus (DM); Lower extremity arterial disease (LEAD); Pulse Oximetry.

**Introduction**

Type 2 Diabetes Mellitus is one of the important risk factors for atherosclerotic Peripheral Vascular Disease (PVD). Diabetes Mellitus (DM) increases the incidence of Lower extremity arterial disease (LEAD) twofold to fourfold [1]. More than 60% of non-traumatic lower-limb amputations occur in people with diabetes [2]. Approximately 15% of individuals with DM develop a foot ulcer and a significant subset will ultimately undergo amputation [3].

In 2004, about 71,000 Non-traumatic lower limb amputations were performed in people with diabetes [2]. Beyond the threat to the limb, these patients face enormous Cardiovascular and Cerebro-vascular risk. With diabetes, tibial vessels below the knee are commonly involved. Because of the pattern of involvement distally, the majority of patients lack classic symptoms, such as claudication. A more devastating consequence of neuropathy is that LEAD patients with diabetes present late, having already developed limb-threatening ischemia with tissue loss, gangrene, or rest pain. The American heart association and American diabetes association recommend annual screening for LEAD in patients with type 2 diabetes and those older than 40 years[4]. Early detection of lower extremity arterial disease (LEAD), before the onset of symptoms in patients with diabetes mellitus, is desirable and can lead to tighter, better control of risk factors for arterial disease. The ideal screening test would be inexpensive, noninvasive, accurate, and easily administered in the physician's office.

Palpation of foot pulses, by itself, is not sensitive and has poor inter-observer variability[5]. The ankle-brachial index (ABI), currently the recommended screening test for LEAD was shown to be a sensitive marker for LEAD[4]. But in diabetes there is increased calcification of vessels, which reduces compliance of vessels so blood pressure may be spuriously high, so false negative reports will be high with ankle brachial index.

Doppler ultrasound methods, such as waveform analysis and duplex color mapping, are accurate but expensive and are not appropriate for screening purposes.

Angiography studies are gold standard but invasive, expensive and compliance in among asymptomatic patients is also poor, hence not appropriate for screening purposes.

Pulse oximeters are widely available in patients care areas and easy to use. The technique of measuring SaO₂ in the blood of a finger doesn’t differ from that of a toe. This technique is noninvasive. Simple to perform. Pulse oximetry will be an effective additional method of screening patients with type 2 diabetes mellitus for LEAD.

**Materials and Methods:**

**Source of the data:**

Asymptomatic Type2 Diabetes Mellitus patients attending outpatient clinic and admitted as inpatients in Dr. B.R.Ambedkar medical college and hospital, K.G.Halli, Bangalore, during recent 2 years were taken up for the study. Clearance has been obtained by the ethical committee of Dr. B.R.Ambedkar medical college and hospital.

**Method of collection of data:**

- Sample size: 50 well established type 2 diabetic patients without any symptoms of lower extremity arterial disease (LEAD) were taken up for the study.
- Study design: cross sectional study

**Inclusion criteria:**

All well established Type2 Diabetes Mellitus who will not have any symptoms of LEAD are enrolled in this study.

**Exclusion criteria:**

1. Age younger than 40 years,
2. Known LEAD or symptoms of LEAD (typical intermittent claudication or rest pain), and
3. Inability to lie supine for the period of testing.
Data was collected in a proforma meeting the objective of the study. A detailed history, general physical, systemic examinations and investigations were done after Informed consent was obtained.

**Instruments:**
1. A Pulse oximetry was used to measure Saturation of Oxygen (SaO2).
2. Systolic blood pressures of the arms and legs were measured with a sphygmomanometer cuff and a handheld 8-MHz Doppler probe.
   We used a standard sphygmomanometer and cuff sizes of 14 cm and 16 cm, according to the size of the arm. And did not use a random-zero sphygmomanometer, because we were interested in the ratio of the blood pressures rather than absolute values. Moreover, most physicians' offices use a standard sphygmomanometer.
3. Doppler waveform analyses of lower extremity arteries were performed using Doppler velocity waveform analysis.

**Procedures:-**
- SaO2 of both big toes with the patients in the supine position and at 12-in elevation of the foot, using a pulse oximetry at room air; and followed by systolic blood pressure of both arms at the elbow and both legs at the ankles in the supine position, using a sphygmomanometer cuff and a handheld Doppler probe.
- The ABI measurements were performed after the pulse oximetry measurements. The ABIs were derived for each leg by dividing the ankle pressure by the higher of the elbow pressures. The ankle pressures were measured using the posterior tibial artery. If the Doppler signal was not obtainable, the dorsalis pedis artery was used.
- All patients also underwent Doppler waveform analysis examination of their lower extremity arteries (femoral, popliteal, tibial, posterior tibial, and dorsalis pedis arteries) by an investigator, who was not aware of the ABI and pulse oximetry results, at a later date in the radiology department.

**Definitions:-**
1. Abnormal pulse oximetry of the toes was defined as a SaO2 value of more than 2% lower than the finger value or a decrease of more than 2% on elevation of the leg (decrease from the value at the supine position).
2. An Abnormal ABI was defined as less than 0.9.
3. For the combination of ABI and pulse oximetry, we defined a positive test result as either an ABI of less than 0.9 or a decrease in SaO2 of more than 2%, as described here in; a negative test result for the combination was an ABI of 0.9 or more and an SaO2 decrease of 2% or less.
4. Significant LEAD was defined as the presence of Monophasic wave forms at anyone of the lower extremity arteries during Doppler waveform analysis. We used Doppler waveform analysis as the standard for comparison. This test has been shown to have a specificity of 97% in the diagnosis of LEAD when compared with Arteriography and has been used as the standard in previous studies of ABI.

**Results**
Fifty Type 2 Diabetes Mellitus (DM) patients who had no symptoms of Lower Extremity Arterial Disease (LEAD) attending OPD and IPD in Dr.B.R.Ambedkar medical college and hospital, Bangalore during recent 2 years were enrolled in this study.

**Table 1: AGE INCIDENCE**

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>40-49</td>
<td>15</td>
<td>30</td>
</tr>
<tr>
<td>50-59</td>
<td>17</td>
<td>34</td>
</tr>
<tr>
<td>60-69</td>
<td>14</td>
<td>28</td>
</tr>
<tr>
<td>&gt;70</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>100</td>
</tr>
</tbody>
</table>

- Maximum age was 75 years and minimum was 41 years.
- Mean age was 56.2±9.478years
- 95% of patient’s fall in the age group of 40-69 years.

**Figure 1: Age incidence**
Table 2: Sex incidence

<table>
<thead>
<tr>
<th>Sex</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td>30</td>
<td>60</td>
</tr>
<tr>
<td>Females</td>
<td>20</td>
<td>40</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>100</td>
</tr>
</tbody>
</table>

Figure 2: Sex incidence

- Male and Female Ratio was 1.5:1

Table 3: Selected Comorbidities in patients with Type 2 Diabetes Mellitus Screened For LEAD

<table>
<thead>
<tr>
<th>Variables *</th>
<th>Valve</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension (HTN)</td>
<td>26(52%)</td>
</tr>
<tr>
<td>Known Coronary artery disease (CAD)</td>
<td>9(18%)</td>
</tr>
<tr>
<td>Known Cerebrovascular Accident (CVA)</td>
<td>4(8%)</td>
</tr>
<tr>
<td>Current Tobacco use (T)</td>
<td>£ 19(38%)</td>
</tr>
</tbody>
</table>

*Data are given as number of patients with documented medical record and treated with medicines
£ Tobacco use within the one month before testing for LEAD.

Duration of Diabetes Mellitus
- The known duration of Diabetes Mellitus ranged from 1-15 years,
- Mean duration of Diabetes Mellitus was 6 years.

Comorbidities in Type 2 DM Screened for LEAD

Out of 50, 26 (52%) had Hypertension, 9 (18%) Known Coronary Artery Disease (CAD), 4 (8%) Known Cerebrovascular Accident (CVA), 19 (38%) Current Tobacco use.

Figure 3: Comorbidities in Type 2 DM Screened for LEAD

The study sample consists of 50 patients (100 extremities) that were examined with all 3 tests pulse oximetry, Ankle-Brachial Index and Doppler waveform analysis.

Table 4: Selected descriptive statistics of ABI and O2 saturation difference of each limb.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right ABI</td>
<td>0.80</td>
<td>1.09</td>
</tr>
<tr>
<td>Left ABI</td>
<td>0.73</td>
<td>1.10</td>
</tr>
<tr>
<td>Right SO2 difference</td>
<td>0.2</td>
<td>3.0</td>
</tr>
<tr>
<td>Left SO2 difference</td>
<td>0.2</td>
<td>3.2</td>
</tr>
</tbody>
</table>

I found significant LEAD (monophasic waveform) by Doppler waveform analysis in 31 (31%) of 100 legs examined. Of that 15 had right and 16 had left leg LEAD. With Pulse oximetry - true positive in 23 (23%) patients, false positive in 2 (2%), true negative in 67 (67%) patients, and false negative in 8 (8%) patients.

With Ankle-Brachial Index - true positive in 20 (20%) patients, false positive in 2 (2%) patients, true negative in 67 (67%) patients, and false negative in 11 (11%) patients. With combination of 2 tests - true positive in 27 (27%) patients, false positive in 4 (4%) patients, true negative in 65 (65%) patients, and false negative in 4 (4%) patients.
<table>
<thead>
<tr>
<th>TEST RESULTS</th>
<th>LEAD *Present No. (%)</th>
<th>LEAD *Absent No. (%)</th>
<th>Sensitivity %</th>
<th>Specificity %</th>
<th>Positive predictive valve</th>
<th>Negative predictive valve</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulse Oximetry Test ψ</td>
<td></td>
<td></td>
<td>74.19%</td>
<td>97.10%</td>
<td>92%</td>
<td>89.3%</td>
</tr>
<tr>
<td>Positive</td>
<td>23</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>8</td>
<td>67</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ankle Brachial Index</td>
<td></td>
<td></td>
<td>60.60%</td>
<td>97.12%</td>
<td>90.9%</td>
<td>87%</td>
</tr>
<tr>
<td>&lt;0.9</td>
<td>20</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥0.9</td>
<td>11</td>
<td>67</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Combination</td>
<td></td>
<td></td>
<td>87%</td>
<td>94.2%</td>
<td>87%</td>
<td>94.2%</td>
</tr>
<tr>
<td>Positive ♂</td>
<td>27</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative £</td>
<td>4</td>
<td>65</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*LEAD as diagnosed by presence of monophasic waveforms in Doppler waveform analysis.
Ψ Positive pulse oximetry test result indicates oxygen saturation at big toe is more than 2% lower than finger saturation or decreases by more than 2% on foot elevation.
♂ Combination positive indicates either positive pulse oximetry test result or ankle-brachial index of less than 0.9.
£ Combination negative indicates negative pulse oximetry test result and ankle-brachial index of 0.9 or higher.

Discussion:
Present study is a cross sectional descriptive study. Fifty Type 2 Diabetes Mellitus (DM) patients who had no symptoms of Lower Extremity Arterial Disease (LEAD) attending OPD and IPD in Dr.B.R.Ambedkar medical college and hospital, Bangalore during recent 2 years were enrolled in this study.
Demographic Profile:

Age group And Sex Ratio

The age group of patient ranged from 41-75 years. Mean age was 56.2±9.478 years. 95% of patients fall in the age group of 40-69 years. Out of 50, 30(60%) were males and 20(40%) were females. Male to Female Ratio was 1.5:1.

G.Iyer Parameswaran et al. a study of 57 patients. Age ranged from 41-84 years. Mean age was 63 years. Out of 57, 27 (47%) were males and 30 (53%) were females. In the present study, male patients had predominated history of Diabetes than females.

Co morbidities

Out of 50, 26 (52%) had hypertension, 9 (18%) known Coronary artery disease (CAD), 4 (8%) known Cerebro vascular Accident (CVA), 19 (38%) current Tobacco use. G.Iyer Parameswaran et al. a study of 57 patients. Age ranged from 41-84 years. Mean age was 63 years. Out of 57, 27 (47%) were males and 30 (53%) were females. In the present study, male patients had predominated history of Diabetes than females.

Hypertension was the most common co morbidity associated with Diabetes mellitus. Few of the patients had macro-vascular complications of Diabetes like CAD & CVA. Tobacco usage was more in our study.

Duration of Diabetes Mellitus

In present study, duration of Diabetes Mellitus ranged from 1-15 years, mean duration of Diabetes Mellitus was 6 years.

G.Iyer Parameswaran et al. duration of Diabetes Mellitus ranged from 1-39 years, mean duration of Diabetes Mellitus was 9 years.

Table 13: Test Results in comparison with other study.

<table>
<thead>
<tr>
<th>Test Results</th>
<th>Present study</th>
<th>G.Iyer Parameswaran et al</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sensitivity</td>
<td>Specificity</td>
</tr>
<tr>
<td>Pulse oximetry</td>
<td>74.14%,</td>
<td>97.12%</td>
</tr>
<tr>
<td>Ankle-Brachial Index</td>
<td>60.60%,</td>
<td>97.12%</td>
</tr>
<tr>
<td>Combination</td>
<td>87%</td>
<td>94.20%</td>
</tr>
</tbody>
</table>

In this study the pulse oximetry of the big toes, at the supine and 12-in elevation positions, is at least as accurate as the ABI in detecting LEAD in patients with type 2 diabetes mellitus.

Pulse oximetry has a Sensitivity of 74.14%, Specificity of 97.10%, and Positive predictive value of 92% and Negative predictive value of 89.3%. ABI has a Sensitivity of 60.60%, Specificity of 97.12%, and Positive predictive value of 90.9% and Negative predictive value of 87.9%. Combination has a Sensitivity of 87%, Specificity of 94.20%, and Positive predictive value of 87% and Negative predictive value of 94.20%.

In comparison, sensitivity of the pulse oximetry is higher than the ABI and specificity is equal for both the tests. The combination of the 2 tests had a higher sensitivity than the ABI but reduced specificity.

The higher sensitivity is desirable in a screening test. G.Iyer Parameswaran and James Dolon study, in Asymptomatic lower extremity arterial disease patients with type 2 diabetes, compared pulse oximetry with ABI as a screening test for detecting LEAD.

They found that Pulse oximetry had a sensitivity of 77% (95% confidence interval [CI], 61%-88%) and a specificity of 97% (95% CI, 91%-99%); ABI had a sensitivity of 63% (95% CI, 46%-77%) and a specificity of 97% (95% CI, 91%-99%). Positive likelihood ratios were 30 (95% CI, 7.6-121) for pulse oximetry and 24.8 (95% CI, 6.2-99.8) for ABI; negative likelihood ratios were 0.23 (95% CI, 0.12-0.43) for pulse oximetry and 0.38 (95% CI, 0.25-0.59) for ABI. For the combination,
sensitivity was 86% (95% CI, 71 %-94%) and specificity was 92% (95% CI, 84%-96%).

Currently recommended screening tests for PAD include pulse palpation and the ABI. Pulse palpation is easy to perform but has interobserver variability. The negative predictive value of a posterior tibial pulse pulse is 96%, but the positive predictive value is only 49% [6]. The dorsalis pedis is congenitally absent in 4 % to 12% of the population.

The ABI has been reported to be very sensitive and specific in patients suspected of having arterial disease [7], but others report that the ABI is not a sensitive test in patients with diabetes mellitus [8].

Previous reports of sensitivity and specificity in excess of 90% for the ABI have involved patients with symptoms and signs of LEAD and have not used ABI strictly as a screening test [9,10]. When used in patients with no symptoms of LEAD, the ABI has been reported to have a sensitivity of less than 30% [11]. The ABI is more sensitive in more severe LEAD.

Carter reported that in patients with severe arterial stenosis on arteriography, the ABI was abnormal in 80%. However, when only mild arterial stenosis was present, the ABI was low in only 50%. This finding suggests that for early detection of LEAD before the onset of symptoms, the ABI may not be as sensitive as reported [12].

Yao et al reported that in patients with angiographically proven stenosis of lower limb arteries, the ABI was less than 1 in 93% of patients [9]. Stoffers et al reported a sensitivity of 87% at an ABI cutoff value of less than 0.92[7].

However, these authors have studied patients with symptoms and signs of LEAD, not asymptomatic patients.

Feigelson et al found that when they excluded patients with symptoms and signs of LEAD, ABI values of less than 0.9 had a sensitivity of only 28.4%. Therefore, the ABI seems less accurate as a screening test in patients without symptoms or signs of LEAD [11]. Moreover, doubts have been cast about the accuracy of the ABI in screening for diabetes, probably due to increased incidence of arterial calcification in diabetes mellitus, which can spuriously elevate the ABI.

The performance characteristics of the ABI as a screening test in patients with diabetes have not been well studied, because most studies of the ABI have include patients with and without diabetes.

Measurement of the tissue oxygen level at the toe by transcutaneous oximetry and toe pulse pressure measurement are more sensitive than the ABI in detecting LEAD in patients with diabetes but need special equipment and training.

Pulse oximetry measures the oxygen saturation of peripheral blood (SaO2). The instrument is commonly available in physicians' offices. Mixed results have been reported with its use in detecting arterial disease in a general group of patients.

Joyce et al [13] reported compared the ABI, pulse oximetry measurement of the toes, and transcutaneous oxygen tension measurement with the arteriographic appearance in patients suspected of having limb ischemia. They found that pulse oximetry correlated best with the arteriographic, appearance that patients with LEAD had significantly lower SaO2 in the ischemic limbs. The SaO2 improved after revascularization.

Jawahar et al [14] studied patients referred to a vascular laboratory with suspected LEAD and a control group not suspected of having LEAD. When an ABI less than 0.9 was considered as LEAD, pulse oximetry had a sensitivity of only 16%. Pulse oximetry results were defined as abnormal if there was a decrease of more than 2% in saturation at the toe from the finger or a decrease of more than 2% on elevation of the foot by 12 inch.

However, this study included patients with and without diabetes and involved patients with symptoms suggestive of LEAD. Moreover, those suspected of having LEAD had further evaluation with Duplex ultrasound scanning of leg arteries, but the control group did not. The authors do not report the comparison of the ABI, pulse oximetry, and duplex scanning results.

The present study differs from the ones cited herein by comparing pulse oximetry and ABI results against a reference test (Doppler waveform analysis) in patients with no symptoms of LEAD. This study results suggest that pulse oximetry is at least as accurate as ABI and is an effective additional method for screening patients with type 2 diabetes mellitus for LEAD.

Pulse oximeters are widely available in patient care areas and easy to use. The technique of measuring SaO2 in the blood of a finger, using a pulse oximeter, is well described and well known. The application of the pulse oximeter probe to the big toe does not differ from that with a finger. The technique is noninvasive. It is commonly used in emergency departments, hospitals, and physician offices during assessment of respiratory and cardiac problems.

Conclusion

In conclusion, these results suggest that pulse oximetry may be a useful additional tool to screen for Lower extremity arterial disease (LEAD) in patients with Diabetes Mellitus.

1. Pulse Oximetry test is Simple and easy to perform in Out-Patients and In-Patients in day to day practice.
2. It has a sensitivity and specificity similar to the Ankle-Brachial Index (ABI), larger studies are needed to confirm how it compares with the ABI.

3. When combined with the Ankle-Brachial Index (ABI), the results for the combination of the 2 tests are superior to those reported for the ABI alone in detecting LEAD in these patients.

4. All patients with Asymptomatic Type 2 Diabetes Mellitus should undergo the screening tests routinely once in 6 months for early detection of Lower extremity arterial disease (LEAD).

5. Assessment of change in clinical outcomes owing to modification of risk factors for Atherosclerosis in Asymptomatic patients identified by screening as having LEAD is an area that needs further research.

Source of Funding: Nil
Source of Conflict: Nil

References: