Presence of Microangiopathy in Type 2 Diabetic Patients Present to Surgical OPD in a Tertiary Care Institute

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Abstract: *This observational study explores the association between diabetic foot ulcers DFUs and microangiopathy among patients with type 2 diabetes mellitus T2DM in a rural medical setting. A total of 100 participants, comprising both diabetic and hyperlipidemic patients, were evaluated using the Ankle Brachial Index ABI to detect peripheral arterial disease PAD. While the study found no statistically significant correlation between the presence of DFUs and microangiopathy, it identified a significant relationship between the duration of diabetes and the development of microangiopathic complications. The findings highlight the importance of early diagnosis through ABI and underscore the need for timely interventions to prevent severe outcomes such as lowerlimb amputation. Proper management of blood glucose and early identification of vascular complications remain critical for improving patient outcomes in diabetes care.*

Keywords: Type 2 diabetes mellitus, diabetic foot ulcer, microangiopathy, ankle brachial index, peripheral arterial disease

1. Introduction

The prevalence of Type 2 Diabetes has been increasing all over the world. There are about 450 million diagnosed and 200 million undiagnosed cases of Diabetes. It is expected that the number of diabetes cases will get doubled in the coming decades.[1]

Diabetic Foot Ulcer has become a serious issue in our community. Diabetic Mellitus is major criteria for causing Diabetic Foot Ulcer [2]. The worldwide prevalence of DFU is 6.3% and it is more common in type 2 diabetes [3]. Diabetic foot ulcers have high significance in morbidity and mortality rates. Mortality rate in DFU is approximately 33%.

Based on several studies it is estimated that one out of four diabetic patients suffer from diabetic foot during their lifetime and only less than 10% patients seek medical help [4]. If diagnosed earlier, it can prevent hospitalization and reduce risks that even include amputation of the lower limb [5]. Awareness about DFU is inadequate among patients and Healthcare providers [6,7], the main characteristic feature of which is a full thickness lesion distal to the ankle [8].

Patients having Peripheral Neuropathy and Microangiopathy are more prone to Diabetic Foot Ulcer [9, 10]. Few finding and studies demonstrate the association between the occurrence of diabetic foot ulcer and Microangiopathy complications including albuminuria and diabetic retinopathy.

Recent study shows that the Frequency of females presented to diabetic clinic was more than males. However, a study carried out in same region has reported prevalence of 11% in males and 9% in females [11].

ABI (Ankle Brachial Pressure Index) is a predictor of microvascular complication which is a chronic complication of diabetes. Early Detection of PAD (Peripheral Artery Disease) helps in preventing serious complications (amputation, impaired functions, low quality of life, mental pressure and depression).[12]

2. Review of Literature

Type 2 diabetes mellitus is a chronic metabolic disease that has an increasing prevalence all over the world. The guidelines of Diabetes Mellitus screening and diagnosis is given by American Diabetes Association (ADA) and World Health Organization (WHO) criteria which comprises of both clinical and laboratory parameter .Till now, no exact cure is known.

The primary risk factor for Type 2 Diabetes mellitus is both lifestyle factors and genetic factors [13]. The lifestyle factors include lack of physical activity, sedentary lifestyle, consumption of alcohol, Cigarrette Smoking.[14]

The genes associated with developing type 2 DM includes, JAZF1, FTO, KCNJ11, NOTCH2, IGF2BP2, TCF7L2, WFS1, CDKAL1, PPARG, SLC30A8, and HHEX. KCNJ11 gene encodes for the islet ATP-sensitive potassium channel Kir6.2, and TCF7L2 (transcription factor 7-like 2) regulates proglucagon gene expression and hence producing glucagon-like peptide-1.[15]

Type 2 DM is characterized by insulin insensitivity as a result of insulin resistance, declining insulin production, and eventual pancreatic beta-cell failure [16,17] and leads to hyperglycemia.

Diabetic microangiopathy is one of the main complications of diabetes mellitus. It refers to the injury caused to the capillary endothelial cells in the retina (retinopathy), mesangial cells of the glomeruli of kidney(nephropathy), and Schwann cells of peripheral nerves (neuropathy) due to oxidative stress. Capillary endothelial injuries causing retinopathy, nephropathy and neuropathy are studied under microvascular complications of diabetes. The signs of these complications appears mostly in patients when management of diabetes has been inadequate. The

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mechanisms of development of diabetic microangiopathy are unknown, but studies suggest that it includes multiple factors such as:

- Genetic factors
- Variation in levels of vasoactive substances
- Changes in vasomotor responsiveness
- Chronic plasma volume expansion
- Tissue hypoxia

Various factors contribute to a state of generalized microvascular vasodilatation in early Type 1 diabetes mellitus which is insulin dependent. This vasodilatation along with the consequent increase in capillary pressures and flows are suggested to be the initiating mechanism that can lead to both renal and extrarenal diabetic microangiopathy. When there are persistent hemodynamic actions on the microvasculature,

- The capillary walls get directly injured
- Promote increased permeability to macromolecules
- Increases capillary wall proliferation
- Thickens the basement membranes
- Narrows the lumens.

These changes causes complete microvascular obstruction and the less damaged capillaries get further vasodilated, thereby ensuring their eventual destruction. The nature of the surrounding tissue affects the kind of ensuing complications. It ranges from reduction of functional reserve, as in skeletal muscle, to the devastating functional consequences seen in organs with endarterial circulation such as the kidney and retina [18]

PAD (Peripheral Arterial Disease) is a general term given to all vascular diseases that can lead to abnormal function and structure of the aorta, its branches, and the lower-limb arteries with pathophysiologies related secondary to atherosclerosis and thromboembolism. [19]

Typically, atherosclerosis decreases the size of the lumen of blood vessels. It leads to deficiencies in arterial perfusion without significant symptoms. However, depending on the degree of obstruction, various symptoms may occur during exercise including claudication, resting pain, ulceration, or gangrene. [20]

PAD is classified according to clinical symptoms. The Fontaine and Rutherford classifications are the most well-known systems, under which severe symptoms are grouped according to increased staging (Table 1) [21, 22, 23]. PAD typically exhibits a chronic course but can be acutely exacerbated. Causes of Acute exacerbation of PAD includes depletion of effective vascular volume by thrombosis, embolism, dehydration, and shock [24]. This acute arterial occlusion is a fatal disease that requires emergent manipulations, such as amputation [19]. The ABI (Ankle Brachial Index) is the standard for the diagnosis of PAD in clinical treatment or epidemiologic studies. ABI is calculated as the **ratio of systolic blood pressure in the brachial artery to that in the posterior tibial artery after resting in a supine position**. It is considered abnormal when it is below 0.90 [19, 24]. It represents a useful resource for the salvage of the lower limb, wound healing and survival prediction of patients [19, 24]. When the diagnostic threshold

was set to 0.90, the sensitivity of ABI for the diagnosis of PAD with >50% stenosis was 95%, and its specificity was 100% [25]. An ABI between 0.51 and 0.90 is considered as a mildly to moderately decreased blood flow, and an ABI <0.50 is evaluated as severely decreased blood flow [19, 24].

$$\text{Right ABI} = \frac{\text{Highest Pressure in Right Foot}}{\text{Highest Pressure in Both Arms}}$$

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The Ankle Brachial Index is an important way to diagnose Peripheral Vascular Disease. This index compares the systolic blood pressure of arms and legs to give a ratio that can suggest severity of peripheral vascular disease.

It has been shown to be a specific and sensitive metric for the diagnosis of Peripheral Arterial Disease (PAD). Additionally, the ABI has been shown to predict mortality and adverse cardiovascular events independent of traditional CV risk factors.

If ABI values were ≤0.9, the patient was diagnosed with angiopathy.

ABI Value	Interpretation	Recommendation
Greater than 1.4	Calcification / Vessel Hardening	Refer to vascular specialist
1.0 - 1.4	Normal	None
0.9 - 1.0	Acceptable	None
0.8 - 0.9	Some Arterial Disease	Treat risk factors
0.5 - 0.8	Moderate Arterial Disease	Refer to vascular specialist
Less then 0.5	Severe Arterial Disease	Refer to vascular specialist

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Aim
To observe the presence of microangiopathy in a patient with type II diabetes attending surgery OPD in a tertiary care institute in rural part of southern India.

Objectives
The major objectives of the conducting study are as follows:
1) To observe the presence of microangiopathy using Ankle Brachial Index in patients with type II diabetes
2) This study is to investigate the association between Diabetic Foot Ulcer and Microangiopathy among the people in rural parts of South India.
3) Association between the Duration of diabetes mellitus and presence of microangiopathy

3. Material and Methods

Study Design: An Observational study

Place of study: Department of General Surgery, Government Villupuram Medical College

Sample Cases: 100 cases

Period of study: 2 months

Inclusion Criteria:
1) Type 2 Diabetic patients
2) Healed or Active ulcer patients
3) Patients with Hyperlipedemia

Exclusion Criteria:
1) Emergency Patients in sepsis requiring Amputations
2) Psychatric patients
3) Patients who are refusing to give consent

Ethical Consideration: After getting approval from institutional ethical committee and informed consent from the subjects, the proforma from case sheets were collected. The study was conducted in tertiary care medical centre in the rural village of Villupuram, Tamilnadu.

After informing the subjects about the objectives of the study and assuring confidentiality of the data collected, written informed consent was obtained from all the subjects before collecting the blood samples.

A detailed history regarding the onset of disease and duration of treatment were recorded. When the patients had histories of intermittent claudication and rest pain, peripheral arterial disease, or absent or reduced pedal pulses, ankle brachial index (ABI) measurements were performed.

The blood samples were taken yo analyse HbA1c, Fasting blood Sugar (FBS), Posr Prandial Blood Sugar (PPBS). The systolic pressures are recorded with a handheld 8-mHz Doppler instrument. Usually a standard blood pressure cuff can be used at the ankle. After recording the systolic pressure at Brachial, Posterior tibial and dorsalis pedis artery, the ABI is calculated. All the above parameters were analysed statistically and tabulated using SPSS software

In this study the presence of Peripheral Artery Disease is found out using Ankle Brachial Pressure Index. To calculate ABI, the systolic pressures are recorded with a handheld 8-mHz Doppler instrument. Usually a standard blood pressure cuff can be used at the ankle. After recording the systolic pressure, then ABI is calculated. ABI of one side is given by highest pressure in same side foot divided by highest pressure in both arms.

The Ankle Brachial Index (ABI) measurements of the patient were analyzed. Every patient rested in a supine position for an at least 5min in a quiet room before the ABI was measured.

The Ankle Brachial Index (ABI) is the systolic pressure at the ankle, divided by the systolic pressure at the arm. The Quantitative variables were expressed as mean +/-standard deviation (S D), whereas qualitative data was presented by frequency and percentages. Student Un paired 't' test was applied to determine the significant difference between the groups. The Logistic regression analysis was done to determine the association of age, gender, duration of diabetes, BMI, HbA1-C, and Peripheral Arterial Disease with DFU. All statistical analysis will be carried at 5% level of significance and P value less than 0.05 will be

considered statistically significant.

4. Observation and Results

Sociodemographic Details
Total 100 subjects were included in the study which included both genders, out of which 12 subjects were euglycemic with hyperlipidemia and 88 persons were type 2 diabetes patients [Figure1].

The 41 subjects were presented with healed or active foot ulcer and 46 subjects were not having Diabetic Foot Ulcer(DFU) [Figure2].
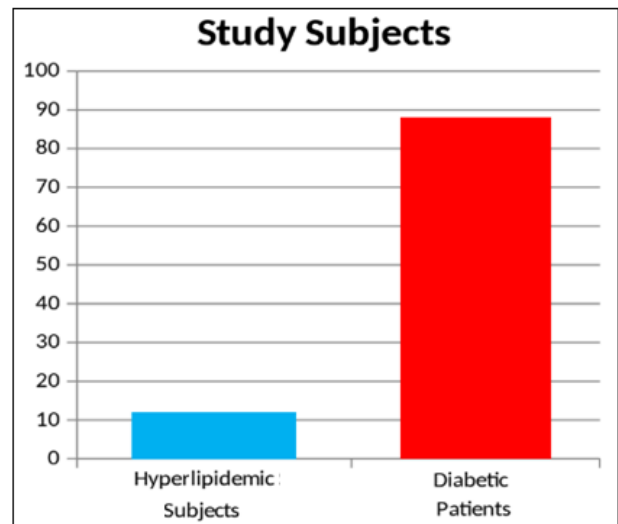
Figure 1: Study Subjects

Hyperlipdemic subjects: 12%
Type 2 Diabetic Patients: 88%
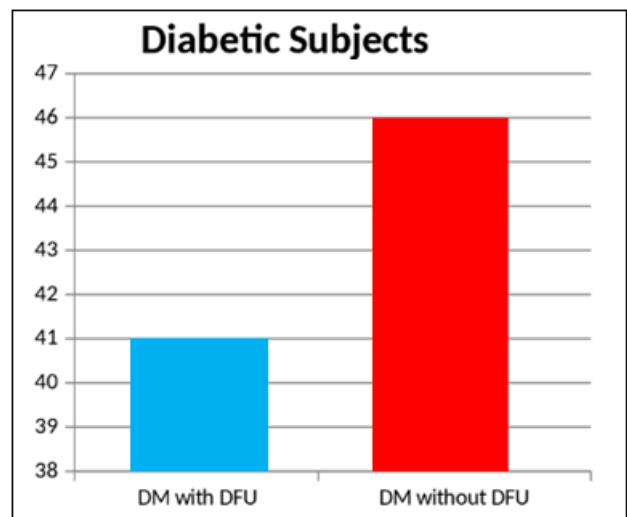
Figure 2: Study Subjects with Diabetes

Subjects With DFU: 41
Subjects Without DFU: 46

Table 1: General Characteristics of the subjects

	Mean	Std. Deviation
Avg. Age	54.93	11.193
Avg. BMI	24.921	1.79293
Avg. Duration of DM	1.79	1.024
ABI[R]	0.9552	0.15406
ABI[L]	0.9654	0.14244
HbA1c	8.17110	1.52662
FBS	162.58	38.3756
PPBS	216.39	54.0945

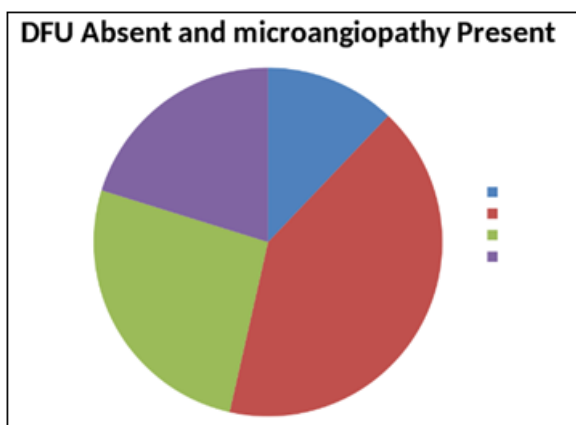Correlation between Diabetic Foot Ulcer & Microangiopathy
Total subjects with Diabetes: 87
Total subjects with DFU: 41
Total subjects without DFU: 46
Total Subjects with DFU and Microangiopathy: 20
Total Subjects with DFU and without Microangiopathy: 21
Total subjects without DFU and with Microangiopathy: 20
Total subjects without DFU and without Microangiopathy: 26

The correlation between diabetic foot ulcer and microangiopathy isn't statistically significant in our study. (Pearson Chi Square value shows the p value of 0.153)
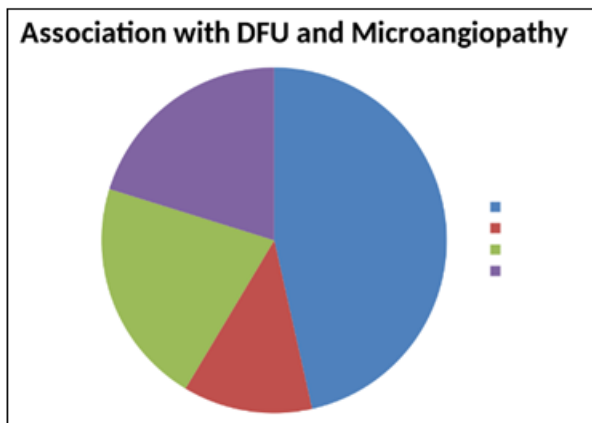
P value= 0.153

The correlation between diabetic foot ulcer and microangiopathy isn't statistically significant in our study. (Pearson Chi Square value shows the p value of 0.153)

Figure 3: Correlation of microangiopathy in type II Diabetic Patients

Correlation Between Diabetic subjects without DFU and having Microangiopathy

Table 2: Correlation Between duration of DM & Microangiopathy

	mic		Total
	Absent	Present	
Duration 0	12	0	12
1	19	11	30
2	17	9	26
3	11	20	31
Total	59	40	99

Duration of Diabetes melltus and microangiopathy is statistically significant and Pearson Chi Square Test shows p value of 0.001

P value =0.001
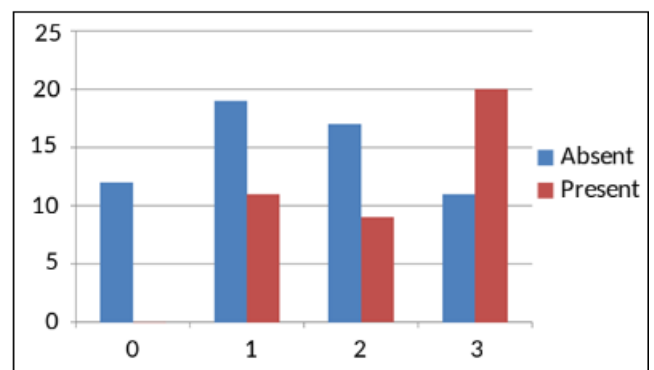
1- No Diabetes
2- Duration less than 5 years
3- Duration Between 5 to 10 years
4- Duration greater than 10 years

Duration of Diabetes Mellitus and Microangiopathy are statistically significant and Pearson Chi-Square test shows p value of 0.001

Table 2: Relationship between BMI, HbA1c, FBS, PPBS and ABI
Group Statistics

Microangiopathy	N	Mean	Std. Deviation	Std. Error Mean
HbA1c				
absent	59	7.2831	1.04801	0.13644
present	40	9.5	1.12387	0.1777
FBS				
absent	59	146.46	32.32503	4.20836
present	40	186.55	34.6469	5.47816
PPBS				
absent	59	184.41	38.9204	5.067
present	40	264.22	35.54015	5.61939

Figure: Relationship between HbA1c and ABI
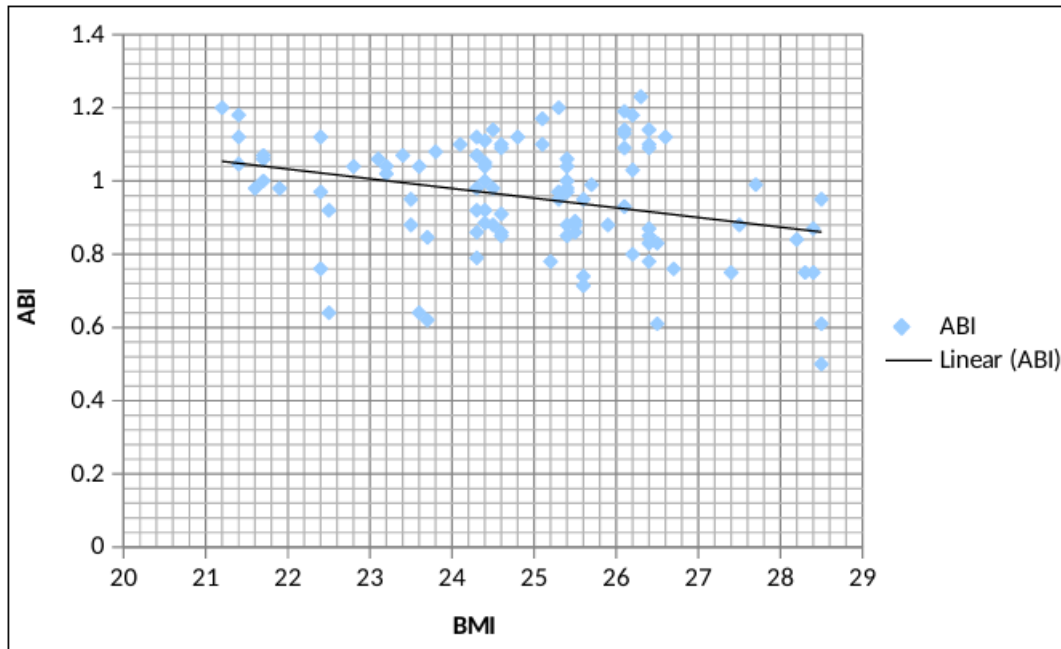
Figure: Relationship between BMI and ABI

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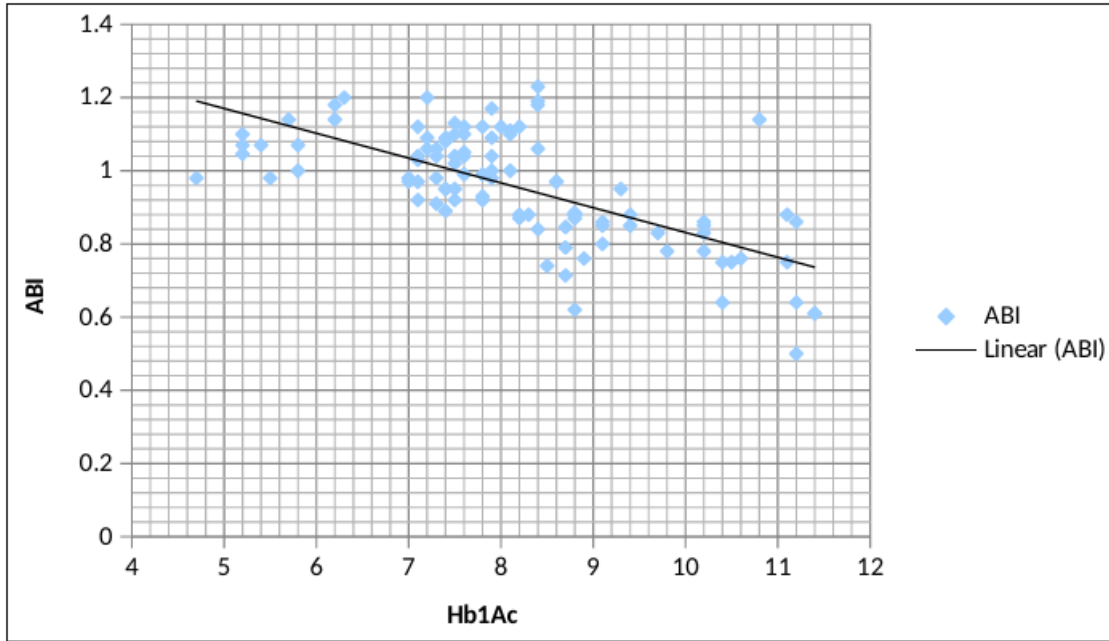Paper ID: SR241013122410   DOI: https://dx.doi.org/10.21275/SR241013122410   440

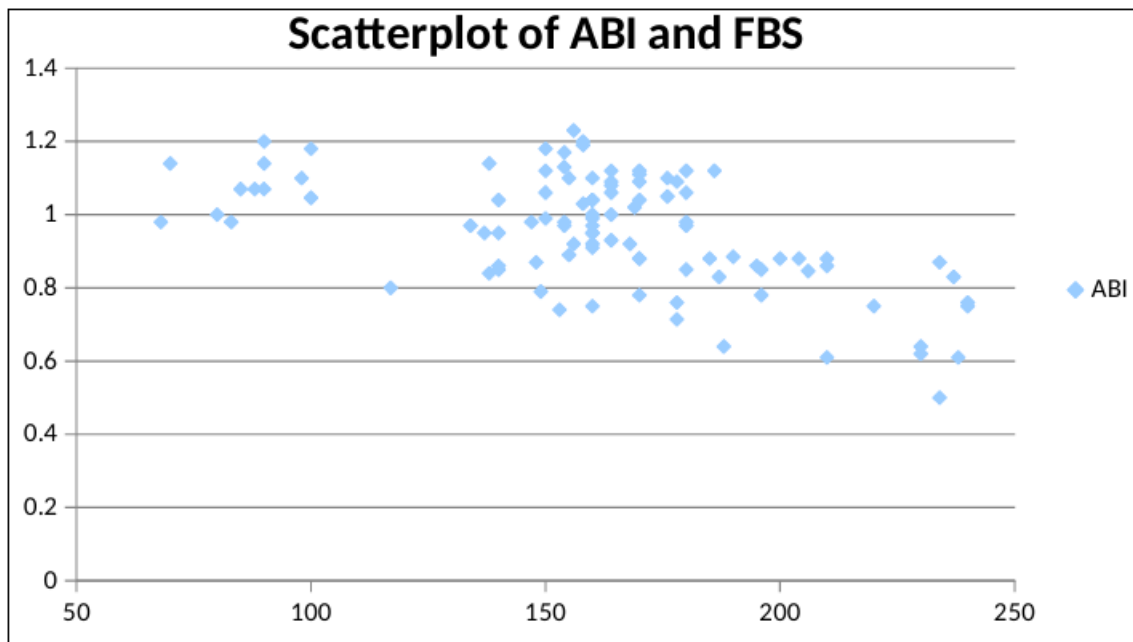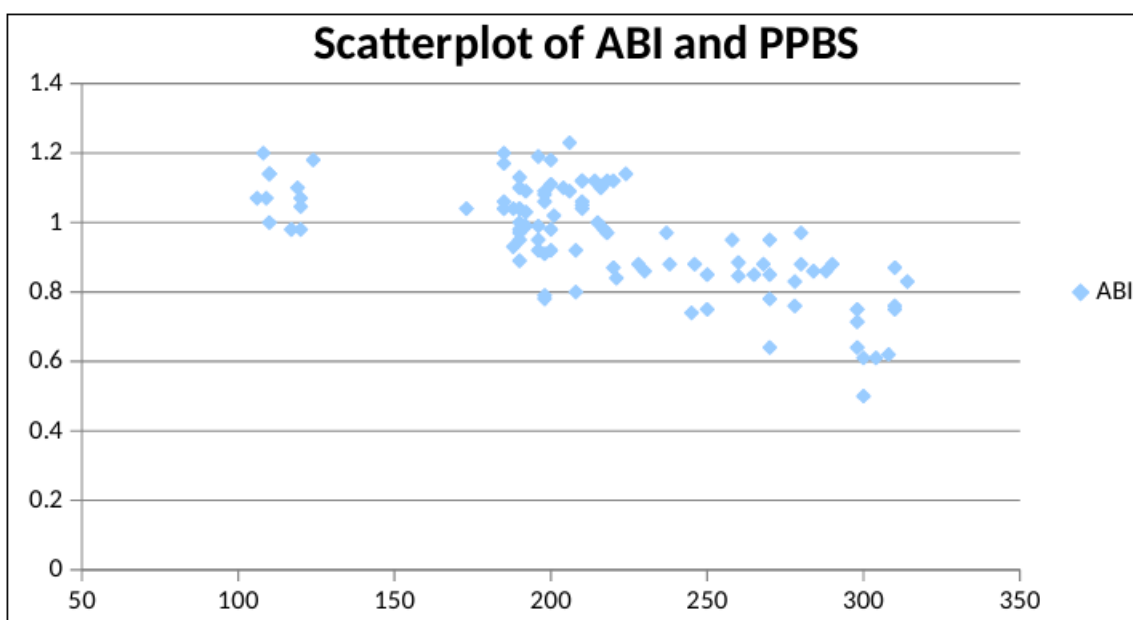**Figure:** Relationship between FBS and ABI

Figure: Relationship between PPBS and ABI

The relationship between HbA1c and ABI, Fasting Blood Sugar (FBS) and ABI, Postprandal Blood Sugar (PPBS) and ABI, BMI and ABI was found to be statistically significant according to the `t' test

In the present study, 100 subjects (one person post amputee) participated, out of which 12 were non diabetic patients with hyperlipidemia and 87 were diabetic patients.

The presence of microangiopathy (peripheral artery disease) was diagnosed in reference with the ABI values of the subjects.

The values of HbA1c, FBS, PPBS were recorded by analyzing the blood samples

Assessment of Incidence of Microangiopathy in Diabetic Patients presents with DFU
Out of the 87 diabetic patients, 41 were having active ulcer and out of which 20 were diagnosed with microangiopathy and PAD and 21 DFU patients were not having microangiopathy and PAD. It was found that there was no significant relation between DFU and incidence of microangiopathy **Assessment of presence of Microangiopathy in Diabetic Patients presents without DFU.** Out of the 87 Diabetic patients, 46 were not having DFU and out of which 26 were presented with microangiopathy and PAD.

Assessment between duration of diabetes and Vascular-Diseases
From this study it is proven that there is a direct correlation between the duration of diabetes mellitus and incidence of microangiopathy and PAD.

The duration of diabetes in 30 diabetic patients were lower than 5 years and they had lower incidence of microangiopathy and PAD as compared to the subjects having diabetes for more than 10 years.

5. Discussion

Tesfamichael G. Mariam, Abebaw Alemayehu,Eleni Tesfaye, Worku Mequannt,Kiber Temesgen, Fisseha Yetwale, and Miteku Andualem Limenih did a study on Prevalence of Diabetic Foot Ulcer and Associated Factors among adult Diabetic Patients and came to a conclusion that higher BMI (overweight and obesity), type of diabetes, neuropathy, and foot self-care practice were factors significantly associated with diabetic foot ulcer. In our study the average BMI is 24.9 and SD is 1.7 and we infer that increasing BMI has negative effect on microvasculature by decreasing values in ABI.

JEHAN SAEED, AMIRA AHMED MAHMOUD, ABEER A. SAEED and NAGLAA A. AHMED conducted a study on the topic 'Ankle Brachial Index As A Monitor of Diabetes Type 2 Microvascular Complications' aimed to find the reliability of Ankle Brachial index in monitoring the microvascular complication of Type II diabetes and the subjects were done clinical evaluation, , measurement of blood pressure and evaluation of fasting & postprandial blood glucose, HbA1c, and ABI and proved that lower ABI was associated with increase level of HbA1c and other sugar parameters. In our study also the evaluation of HbA1c was done and the mean value of HbA1c in subjects with microangiopathy was 9.5 and the negative correlation was proved.

EDGAR J.G. PETERS, MD LAWRENCE A. LAVERY, DPM, MPH evaluated the effectiveness of a diabetic foot risk classification system by the "International Working Group on the Diabetic Foot" to predict clinical outcomes and found out the foot risk classification of the "International Working Group on the Diabetic Foot" predicts ulceration and amputation and can function as a tool to prevent lower extremity complications of diabetes. Masuomi Tomita, Yusuke Kabeya, Mari Okisugi, Takeshi Katsuki, Yoichi Olkawa, Yoshihito Atsumi, Kempei Matsuoka, Akira Shimada did research on Feb,2016 to determine if Diabetic Microangiopathy Is an Independent Predictor of Incident Diabetic Foot ulcer.as a retrospective cohort study of 1305 patients with type 2 diabetes who were assigned to the following groups Category 1- normoalbuminuria without DR (n = 712). Category 2. Alb with Dr (n = 95) Category 3- normoalbuminuria With DR (n =185) and Category 4. Alb with DR (n 273). Results showed 50 subjects developed diabetic foot ulcers. With Incidence rates of 1.6/1000, 1.5/1000, 3.4/1000 and 12.5/1000 in Categories 1. 2. 3. and 4 respectively indicating that presence of DR and Alb Significantly Increases the risk of diabetic foot ulcer development.

Prospective study on microangiopathy in type 2 diabetic foot ulcer by Fabio Flordaliso, Clerici, Serena Maggioni Maurizio Caminiti, Clnzia Bisighini, Deborah Novelli, Daniela Minnella Alessandro Corbelli. Riccardo Morisi, Alberto De loca, Ezio Faglia. investigated the significance of microangiopathy in the development of foot ulcer by histological analysis of capillary ultrastructure. They concluded that Capillary Microangiopathy is present in equal measure in neuroischaemic and neuropathic diabetic footskin.

In our study the correlation between microangiopathy and presence of foot ulcer is not statistically significant though numerically the presence of microangiopathy is more in patients with diabetic foot ulcer statistical significance may need study on larger sample size.

Claudia R. L. Cardoso & Juliana V. Melo & Guilherme C. Salles & Nathalie C. Leite & Gil F. Salles aimed to evaluate the relationship between the ABI and the occurrence of micro- and macrovascular complications in individuals with type 2 diabetes and came to a conclusion that low ABI is associated with excess risk of adverse cardiovascular outcomes, mortality and peripheral neuropathy development or worsening, and improves cardiovascular risk stratification. The ABI should therefore be routinely evaluated in individuals with type 2 diabetes.

In our study the average ABI value on R leg is 0.95 and on L leg is 0.96.

Ankle-brachial index and peripheral arterial disease: An evaluation including a type 2 diabetes mellitus drug-naive patients cohort research done by Joao Soares Felicio, Camila Cavalcante Koury, Nathalie Abdallah Zahalan, Fabricio de Souza Resende, Manuela Nascimento de Lemos, Rafael Jardim da Motta Correa Pinto, Norberto Jorge Kzande SouzaNeto, Isabela Imbelloni Farias de Franco, Maria Clara Neres lunes de Oliveira, Angelica Leite de Alcantara, Ana Carolina Contente Braga de Souza, Marcia Costa Dos Santos, Natercia Neves Marques de Queiroz, Luciana Marques da Costa Farias, Danielle Dias da Silva, Karem Mileo Felicio, Franciane Trindade Cunha de Melo, Joao Felicio Abrahao Neto on 711 subjects showed that in type 2 diabetes mellitus ankle-brachial index should be measured for diagnosis.

In addition sedentary lifestyle was strongly associated with the presence and severity of peripheral arterial disease. "Non-invasive vascular assessment in people with type 2 diabetes: Diagnostic performance of Plethysmographic- and-DoppIer derived ankle brachial index, toe brachial index, and pulse volume wave analysis for detection of peripheral arterial disease" by Mohammad Reza Babael, Mojtaba Malek, Fatemeh Tajik Rostami, Zahra Emami, Nahid Hashemi Madani , Mohammad Ebrahim Khamseh Concluded that Within a population Of patients with T2DM, TBI less than 0.38 provided the best sensitivity for detection of PAD followed by PVW,ABI < or equal to 0.9.

JEHAN SAEED, M.D.; AMIRA AHMED MAHMOUD, M.D.; ABEER A. SAEED, M.D. and NAGLAA A. AHMED, M.D. did a cross sectional study to find whether Ankle-brachial index could be a useful monitor of development of micro vascular complications in type 2 diabetes and they found out that Low ABI is common in patients with T2D and found that ABI screening should be performed in diabetic population for early evaluation of

microvascular complications.

Critical analysis and limitations of resting ankle brachial index in the diagnosis of symptomatic peripheral arterial disease patients and the role of diabetes mellitus and chronic kidney disease was studied by Ali F AbuRahma, Elliot Adams, Joseph AbuRahma, Luis A Mata, L Scott Dean, Cristyn Caron, Jennifer Sloan in patients and showed that of symptomatic patients with PAD with 50% or greater stenosis had normal or inconclusive ABI.

The reliability of the ankle brachial index: a systematic review was done by Sarah Casey, Sean Lanting, Christopher Oldmeadow, Vivienne Chuter to examine the inter- and intra-rater reliability of the ABI as it is widely used in clinical practice as a noninvasive method to detect the presence and severity of PAD and concluded that the inter- and intra-tester reliability of the ABI is acceptable.

Interpretation and significance of ankle-brachial systolic pressure index, a study by Sae Hee Ko , Dennis F Bandyk using a sphygmomanometer and continuous-wave Doppler probe concluded that Measurement of ABI is recommended as the initial diagnostic test for patients with exertional leg pain claudication, to assess the healing potential of foot lesions after blunt extremity trauma to detect occult arterial injury, and as part of the routine health assessment of patients with diabetes and peripheral arterial disease.

In our study clinical signs of ischemia were present in 41 and among them 20 persons present with low ABI which infer that ABI is a good modality for screening diabetic patients for presence of microangiopathy.

K Dahl-Jorgensen did a study on Diabetic microangiopathy and concluded that common Microvascular complications of diabetes include retinopathy, nephropathy and neuropathy. The mechanisms by which diabetic Microangiopathy develop are not known, but probably include genetic influences and several biochemical changes. The structural hallmark of diabetic microangiopathy is the thickening of the capillary basement membrane.

These changes may lead to Occlusive angiopathy and to tissue hypoxia and damage. There is a curvilinear association between the risk of development and progression of microangiopathy and mean blood glucose.

In our study average fasting blood glucose is 162.58 and post prandial glucose is 216.3 also in our study the presence of microangiopathy in the form of lower ABI was found in patient with higher level of glucose and their average mean was 186.5 fasting glucose and post prandial was 264.2

Jonathan M Firnhaber, C S Powell conducted a study on Lower Extremity Peripheral Artery Disease: Diagnosis and Treatment and came to a conclusion that the duration of diabetes is a risk factor for the development of PAD.

In our study the average duration of illness is 8yrs and the complications such as microangiopathy is significantly correlated with duration of the illness with p value 0.001

6. Conclusion

In low and middle income countries where the incidence of Diabetes Mellitus is greater face the greatest burden of the disease. People living with disease in these underdeveloped countries s have limited access to proper treatment and management, which leads them at risk of developing chronic complications of the disease like small-vessel complications. Microvascular and macrovascular complications are a major outcome of the metabolic syndrome that adversely influences the quality of life and also they impose a great burden on the patient and the healthcare service providers. Therefore, the early diagnosis of the small vessel disease will guide health service makers in the prevention and help the clinicians in managing their efforts.

7. Summary

100 subjects has participated in our study.

In our study the mean age of the subjects were found to be 54.93 with a standard deviation of 11.19, the mean BMI of the subjects were found to be 24.9 with a standard deviation of 1.709. The ABI was measured to find the microangipathy of the subjects and the mean ABI [R] was 0.95 and ABI [L] was found to be 0.96. The mean HbA1c, FBS, PPBS was found to be 8.1, 162, 216 respectively.

In this study the correlation between DFU and microangipathy was found to be statistically insignificant and the correlation between the duration of type II diabetes and microangipathy was found statistically significant.

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