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Electrical Impedance Study in Diabetes Mellitus

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Abstract: Diabetes mellitus has raised concerns about structural and functional changes in blood cells, as well as changes in blood impedance. The purpose of this study is to investigate the relationship between electrical impedance values measured with the Bioelectrical Impedance Analyzer (BIA) in diabetes patients. Blood samples were collected from 5 healthy people and 5 diabetes patients for the study. Electrical impedance testing with a BIA. The impedance method determines the electrical properties of blood by measuring its resistance and reactance at various frequencies. The results of the BIA are analyzed and compared to body health parameters such as the blood glucose level index. The average electrical impedance value in diabetes mellitus patients measured at a frequency of 100 Hz to 100 kHz with a current injection of 10 μA was found to be lower than the average electrical impedance value in healthy people. This study shows that the electrical impedance value of diabetes mellitus patients is lower than the impedance value of healthy people. This is consistent with diabetes mellitus patients' blood glucose levels, which are higher than healthy people's blood glucose levels.

Keywords: BIA; Diabetes; Electrical; Impedance

Introduction

Diabetes mellitus is a chronic disease characterized by elevated blood sugar (glucose) levels (Alam et al., 2021). In the human body, blood glucose balance must be considered. Blood glucose levels that are too high or too low are harmful to the body (Bolla & Priefer, 2020; Manoharan et al., 2023). High blood sugar levels are linked to cardiovascular disease, blood vessel disease, eye disease, kidney disease, tooth decay, and nerve damage (Gonzalez-Correa et al., 2019; Kumar et al., 2020). Diabetes causes nerve damage when blood sugar and blood pressure levels are too high. This can result in digestive issues, erectile dysfunction, and other issues (Akhtar et al., 2023). Diabetes mellitus diagnosis is critical because diabetes is a chronic disease with serious health consequences if not treated properly (Banday et al., 2020; Sharma et al., 2010).

In general, a blood glucose level test, oral glucose tolerance test (OGTT), HbA1c test, random blood glucose examination, and urine examination are used in the clinical diagnosis of diabetes mellitus (Casadei et al., 2021). Because this diabetes detection method is still invasive, non-invasive methods are required. The Bioelectrical Impedance Analyzer (BIA) is a non-invasive, compact, portable device that can produce the entire spectrum based on impedance values (Portugal et al., 2020; Silva-Tinoco et al., 2021). This non-invasive method is used to reduce the estimated value of a pricked finger in order to prevent infection, where the impedance value is affected by blood glucose levels (Eke et al., 2020; Machino et al., 2021). As a result, it is hoped

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that this tool will be able to supplement existing clinical tests.

This is an observational study that employs impedance methods. Diabetes patients' blood quality is determined by the electrical impedance value (Elblbesy, 2019). This study included five diabetes patients and five healthy people as controls. The goal of this study was to look at electrical impedance values in diabetes patients. The results will be compared to electrical impedance and blood glucose levels in diabetes patients and healthy people.

The Bioelectrical Impedance Spectroscopy (BIS) tool is used in this study, which has several advantages, including the fact that it does not make the patient sick because it does not come into direct contact with the human body when measuring blood samples (Hossain & Dhar, 2013). It is also safe, fast, easy, cost-effective, and effective (Torres et al., 2023). Aside from that, this tool can be used as an early detection tool to determine whether or not diabetes mellitus patients are at risk of complications by examining their electrical impedance value (Omura-Ohata et al., 2019).

Method

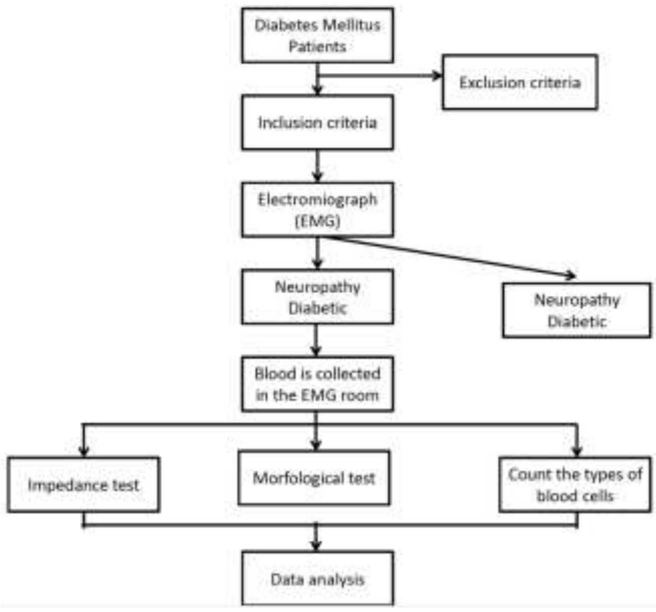


Figure 1. Research flow diagram

At RSUD Dr. Saiful Anwar Malang, this study passed the ethical requirements with reference number 400/186/K3/302/2023. This is a form of observational research. The study included 5 diabetes patients from RSUD Dr. Saiful Anwar Malang and 5 healthy people as controls. The study was carried out between September 4 and November 6, 2023. Blood was drawn from a population of diabetes mellitus patients who met the inclusion criteria (aged 40-75 years, mentally and physically healthy, a history of DM > 5 years, a history of type 2 DM). The inclusion criteria are suffering from serious complications (suffering from more than one type of complicated disease) and the exclusion criteria are willing to be a respondent. Figure 1 depicts a research flow diagram.

An impedance measuring device, namely BIA, with a frequency range of 10 Hz - 100 kHz and an injected current of 10 µA is used to determine the electrical impedance value (Tronstad et al., 2022).

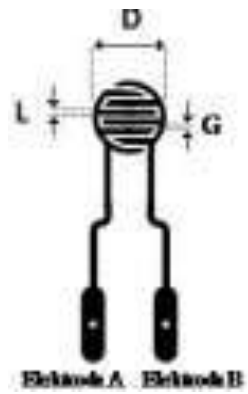
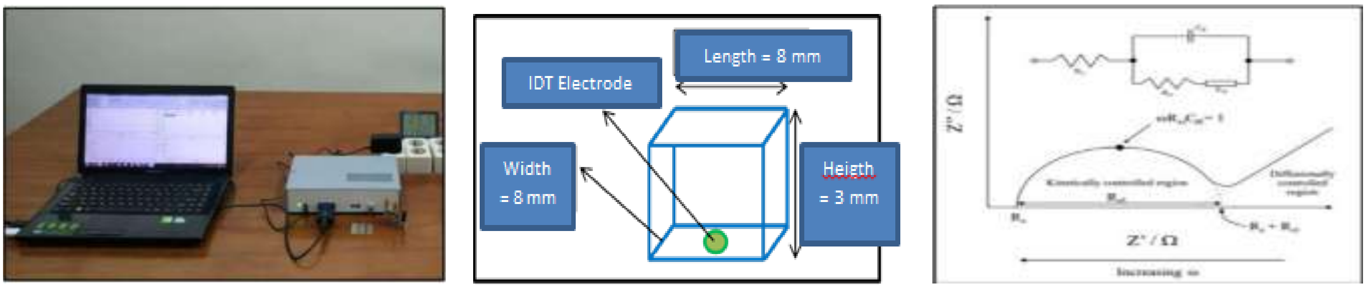


Figure 2. Interdigital transducer (IDT)

The electrode design of the Interdigital Transducer (IDT) is shown in Figure 2. IDT is a tool that acts as an input, converting voltage variations into mechanical acoustic waveforms. When an AC voltage signal is applied to the IDT, it generates acoustic waves that propagate along an axis perpendicular to both directions of the finger.

Figure 3 (a) depicts a research series made up of various components such as a laptop loaded with the BISDAQ application, cables, and BIA tools. A voltage source, calibrator, and electrodes are included in this BIA tool. The calibrator is linked to the laptop to view the results of the impedance graphic display, the electrode serves as the sample medium, and the voltage source is powered up. Figure 3 (b) depicts a sample container with dimensions of 8 mm long, 8 mm wide, and 3 mm high. The Interdigital Transducer (IDT) electrode is located in the center of the container design. When the data fitting process is used to determine the equivalent circuit model, the results of electrical impedance measurements in blood are analyzed. The equivalent circuit model used in this study is the standard Randles circuit model. The fitting procedure is carried out by identifying the Randles model's element values. Figure 3 (c) shows how to identify element values in the Randles model.



(a) (b) (c)

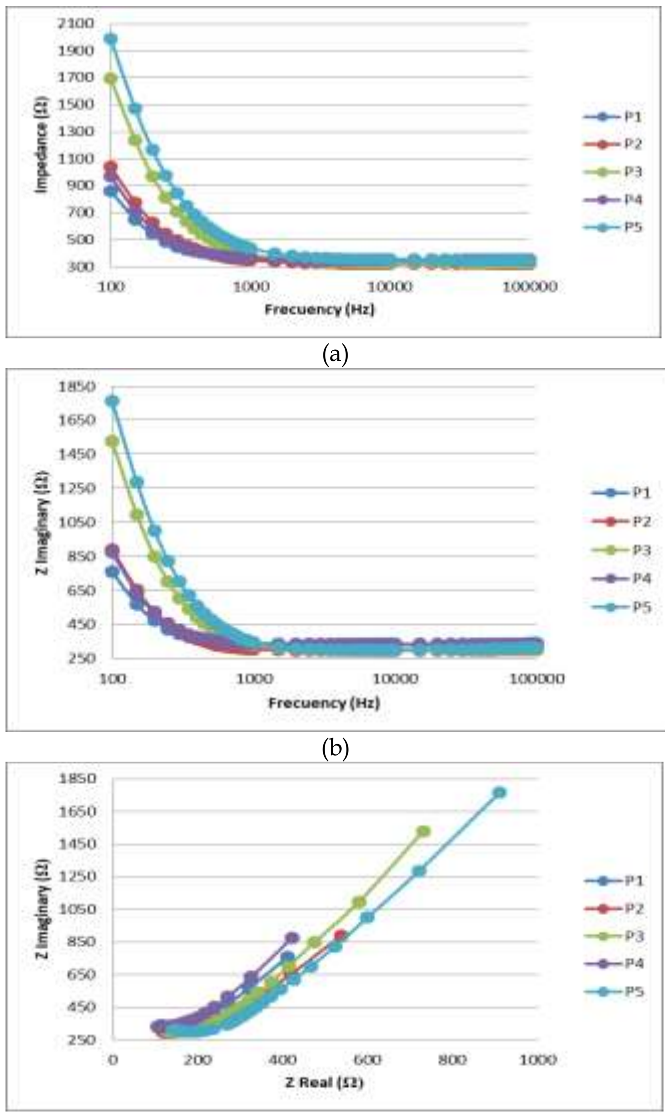
Figure 3. (a) Research design. (b) Design of sample container. (c) How to determine the value of each element of the Randles (Sun et al., 2021)

Result and Discussion

Impedance measurements were performed with a current injection of 10 µA in the frequency range 100 Hz to 100 kHz. Figure 4 (a) depicts a frequency function-based graph of diabetes patients' impedance. Based on this graph, it can be seen, that the electrical impedance value decreases between frequencies of 100 Hz and 1000 Hz, while the graph appears straight or stable between frequencies of 1000 Hz and 100 kHz.

The impedance value measured in first diabetes patient (P1) was 864.0 at 100 Hz (lowest frequency) and decreased logarithmically to 357.0 at 100 kHz (highest frequency). Second diabetes patient (P2) had an impedance value of 1040.3 at the lowest frequency and experienced a logarithmic decrease to 323.6. The impedance values measured in third diabetes patient (P3) ranged from 1694.7 at the lowest frequency to 331.2 at the highest frequency. At the lowest frequency, fourth diabetes patient (P4) had an impedance value of 970.5 and at the highest frequency, it was 349.4. Fifth diabetes patient (P5) had an impedance value of 1986.6 at the lowest frequency and 346.9 at the highest frequency. The electrical impedance value in the blood of diabetes patients varies due to many factors such as the patient's level of neuropathy, medical history, and other test results that detail the patient's condition (Lyons-Reid et al., 2021; Sun et al., 2021). Figure 4 (a) shows that when the frequency is greater than 5 kHz, the impedance values measured from 5 blood samples tend to be relatively stable.

Figure 4 (b) depicts an imaginary Bode Z plot of diabetes patient data from 5 samples. The Z imaginary value is calculated by multiplying the Z value with the phase difference sine (Z sin φ) (Drab et al., 2020). The measured blood impedance values represent both real and imaginary parts. Capacitance, the imaginary part of the impedance, varies greatly with frequency (Pouragha et al., 2021). The measured capacitive reactance value will be higher if the given frequency is close to zero, and lower if the given frequency is higher, causing the measured impedance value to decrease. Equation 1 can be used to calculate capacitive reactance (Xc) (Schofield et al., 2020).



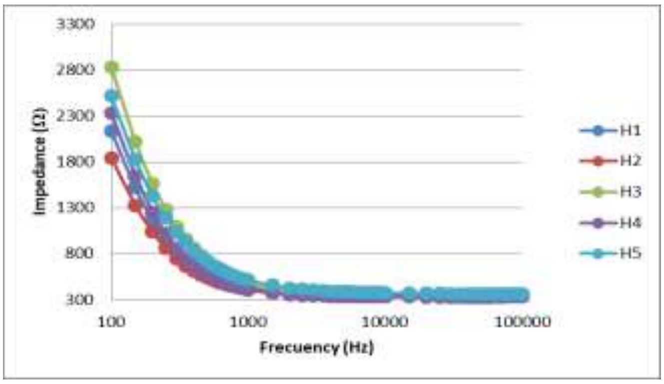
(a) (b) (c)

Figure 4. Graph of Electrical Response (Impedance) of Whole Blood Cells in Diabetes Mellitus Patients. (a) Bode plot of impedance of diabetes mellitus patients. (b) Z Imaginary Bode plot of diabetes mellitus patients. (c) Nyquist plot of diabetes mellitus patients in the five samples

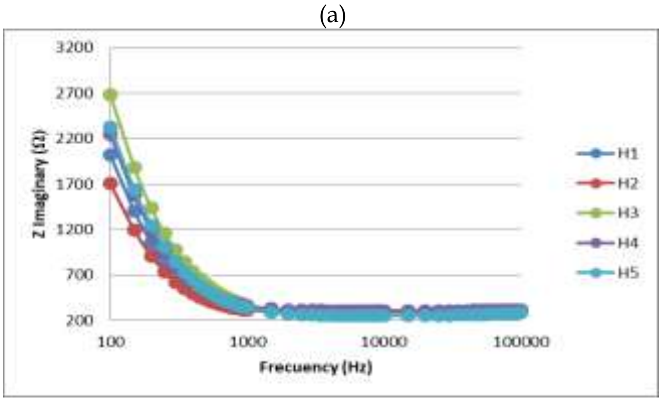
$$Xc = \frac{1}{2\pi C} \quad (1)$$

Xc is capacitive reactance, f is frequency, and C is capacitance. Equation 1 shows that capacitive reactance (Xc) varies inversely with frequency (f). As the frequency increases, the capacitive reactance decreases.

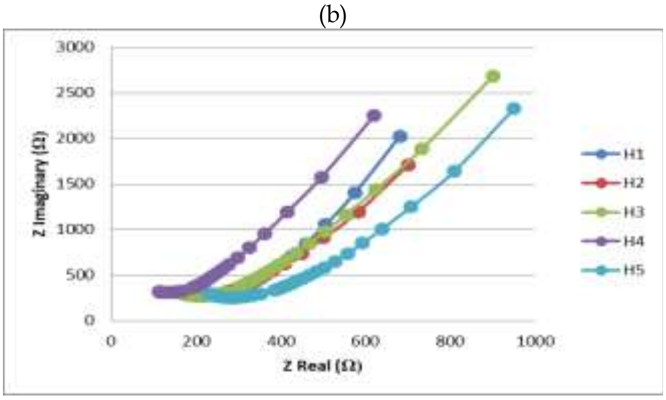
Figure 4 (c) depicts the Nyquist graph for the five diabetes mellitus patient samples. At a frequency of 30 kHz, the first intersection point on the x-axis of the nyquist graph (Z real) indicates a series of medium resistances originating from solution resistances in the electrolyte resistance, separator, and external circuit (Machino et al., 2021; Sucipto et al., 2016).



(a)



(b)



(c)

Figure 5. Graph depicting the electrical response (impedance) of whole blood cells in healthy individuals. (a) Control data impedance bode plot. (b) Z Imaginary Bode plot of control data (c) Nyquist plot of control data in the five samples

A bode plot of impedance in healthy people is shown in Figure 5 (a). This graph shows that the average range of impedance values for healthy people is between 1800 and 2800. Each healthy person's impedance value decreases at frequencies ranging from 100 Hz to 1000 Hz and remains stable at frequencies ranging from 1000 Hz to 1000 kHz. The impedance value measured in the first healthy people (H1) was 2135.6 at 100 Hz (lowest frequency) and decreased logarithmically to 354.1 at 100 kHz (highest frequency). The second healthy people (H2) has an impedance value of 1847.5 at 100 Hz or the lowest frequency and decreases logarithmically to 344.5 at 100 kHz or the highest frequency. Data from the third healthy people (H3) to the fifth healthy people (H5) have impedance values of 2832.5, 2334.4, and 2517.5 at the lowest frequency, and 335.9, 334.9, and 368.4 at the highest frequency. The electrical impedance values in the blood of healthy people or control data do not differ significantly because the factors influencing healthy people are fewer than those influencing diabetes mellitus patients, such as the age of control data respondents (Prasad & Roy, 2020). Because the ages of the respondents as control data are not significantly different, the resulting electrical impedance values are also not significantly different. The graph below depicts the relationship between frequency and phase difference in control data (Lyons-Reid et al., 2021).

Figure 5 (b) depicts the relationship between frequency and imaginary Z in normal people. The average impedance value of five normal people ranges from 1700 Ω to 2700 Ω. At frequencies ranging from 100 Hz to 100 kHz, the impedance appears to decrease, whereas at 1000 Hz to 100 kHz, it appears to remain stable or decrease. The measured capacitive reactance value will be higher if the given frequency is close to zero, and lower if the given frequency is higher, causing the measured impedance value to decrease (Dubiel, 2019). The real part of impedance, resistance, is not frequency dependent. The Z real value is calculated by multiplying the Z value by the cosine of the phase difference (Z cos φ), as illustrated in figure 5 (b) (Grossi & Riccò, 2017).

Figure 5 (c) depicts a Nyquist graph, with the x-axis representing the real impedance (Z real) and the y-axis representing the imaginary impedance (Z imaginary). At intermediate frequencies, a straight line with a specific slope appears; the impedance represents ion diffusion in the electrode surface structure At low frequencies, the measured sample impedance exhibits capacitor-like behavior in a pure electrical double layer, indicated by a vertical line (Ariyoshi et al., 2022).

The blood glucose levels in all diabetes mellitus patients are shown in Table 1. Normal blood glucose levels range between 70 and 130 mg/dL. Table 1 demonstrates that P4 has the highest blood glucose levels. This can be caused by the body's inability to effectively utilize glucose, resulting in excess glucose production (Wang et al., 2021). Influencing factors include insulin resistance, insufficient insulin production, excessive glucose production, and other hormonal disorders (Bolla & Priefer, 2020). Electrical impedance values can be affected by blood glucose levels. High blood glucose levels can alter the distribution of bodily fluids (Kamat et al., 2014). Diabetes mellitus patients frequently suffer from dehydration or changes in body fluid composition, both of which can impair electrical conductivity. This can be used to represent the electrical impedance value (Deischinger et al., 2020; Pedro et al., 2020).

A glucometer was used to measure blood sugar levels in diabetes mellitus patients and healthy people (Figure 6).

Figure 6. Glucometer

A glucometer works by using an enzymatic reaction to generate an electrical or optical signal that can be measured and converted into a glucose level. In this study, a small blood sample was drawn, and then a drop of blood was placed on the glucometer test strip. The glucometer detects the signal generated by the chemical reaction on the test strip and converts it into a blood glucose level value in milligrams per deciliter (mg/dL) (Salacinski et al., 2014). The following are the blood glucose levels in diabetes and healthy people.

Table 1. Blood Glucose Levels in Patients with Diabetes Mellitus

Patients	Blood glucose levels
P1	135 mg/dL
P2	138 mg/dL
P3	212 mg/dL
P4	282 mg/dL
P5	452 mg/dL

As controls, the blood glucose levels of all healthy people are shown in Table 2. Healthy people's insulin hormones function normally, allowing them to regulate their blood glucose levels (Aleixo et al., 2020). The measured impedance value is affected by the quality of blood cells in each sample used in this study. The results of a complete blood test and a peripheral blood smear can be used to determine the quality and quantity of blood (Ulubeli et al., 2020).

Table 2. Blood Glucose Levels in a Healthy People

People	Blood glucose levels
H1	98 mg/dL
H2	103 mg/dL
H3	110 mg/dL
H4	120 mg/dL
H5	121 mg/dL

The arrangement and properties of the blood cell membrane, which has an electrical charge and can cross the plasma membrane, influence impedance (Nicolson, 2014). The membrane's contents are made up of K^+ ions, the cation content of which is protein and other dissolved substances. Outside the membrane, sodium ions (Na^+) are present, and the anion structure is chloride (Prasad & Roy, 2020; Risinger & Kalfa, 2021). Cell membranes are made up of hydrophilic phospholipid heads and a variety of proteins that can store current. The cell membrane has capacitor-like properties, whereas the phospholipid tail is hydrophobic and contains non-electrolyte lipids that can inhibit incoming current (Hess, 2014). In blood cells, capacitors and resistors located in the membrane and internally of the cell determine the cell's reactance (Drab et al., 2020).

The electrical impedance value is also affected by the mobilization and randomness of charges and ions in the blood, as well as the dominance of processes occurring at the electrode material's interface (Li et al., 2021). The results of measurements in the frequency range of 100 Hz to 100 kHz are described as relaxation of non-permanent dipoles formed in the flow of ions on the cell surface, the values of which depend on the complex intracellular and membrane surfaces (Berzuini et al., 2021).

Conclusion

Diabetes mellitus patients had lower average electrical impedance values (100 Hz to 100 kHz, 10 μA current injection) compared to healthy individuals. According to this study, diabetes mellitus patients have lower electrical impedance values than healthy people. This is consistent with the higher blood glucose levels of diabetics compared to healthy people. The frequency or current used influences the results of electrical impedance tests for diabetes and healthy blood. It would be preferable for the next study to ensure that all patients' conditions are as similar as possible (no one is taking medication before blood glucose levels are measured), so that medication consumption has no effect on blood glucose measurement.

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Conceptualization, L.A.P and C.S.W.; methodology, L.A.P., E.R., S.N.K., H.S. and A.G.; software, C.S.W.; validation, A.W.S. and C.S.W.; formal analysis, L.A.P. and A.W.S.; investigation, L.A.P.; resources, E.R., S.N.K., H.S. and A.G.; data curation, L.A.P..; writing—original draft preparation, L.A.P.; writing—review and editing, A.W.S.; visualization, L.A.P.; supervision, C.S.W.; project administration, L.A.P. and C.S.W.; funding acquisition, L.A.P. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest
The authors declare no conflict interest.

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