

Cover Page for Protocol

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Effect of Moringa leaf capsules on glycemic control of Type 2 diabetic patients: A Randomized Controlled trial.

Introduction:

Diabetes mellitus (DM) is one of the most common public health concerns around the globe. It is a disorder of carbohydrate metabolism in which blood glucose level is chronically high due to insulin's impaired secretion or action. Out of 463 million adults worldwide who suffer from diabetes, 90% of these people suffer from type 2 diabetes mellitus. According to the International Diabetes Federation, in year 2022, 26.7% of adults in Pakistan are a victim of diabetes mellitus, making the total number of cases approximately 33,000,000. ⁽¹⁾

This alarmingly high number not only poses an enormous risk of health complications, but also a huge financial load on patients. A substantial proportion of patients' income is spent on diabetes care. The mean annual direct cost per patient with diabetes was estimated to be PKR 80,000. Medications accounted for the largest share (60.4%) of this cost. Age, locality, high socioeconomic status, and prolonged disease duration were significantly associated with the direct costs of illness ($p < 0.05$). Furthermore, 19% of total earnings among very low-income patients were spent on diabetes care. ⁽²⁾

According to the World Health Organization (WHO), traditional medicine is defined as "health practices, approaches, knowledge and beliefs incorporating plant, animal and mineral based medicines, spiritual therapies, manual techniques and exercises, applied singularly or in combination to treat, diagnose and prevent illnesses and maintain well-being." The WHO has supported the evaluation of medicinal plants and herbs for the management of certain chronic conditions ⁽³⁾

In the recent years there has been an exponential growth in the field of herbal medicines and the demand of these is increasing both in developing and developed countries because of their natural origin, less side effects and low cost. ⁽⁴⁾

The effects of some herbal therapies, such as cinnamon, fenugreek, and milk thistle, on hyperglycemia in patients with type 2 diabetes have been investigated in clinical trials, with mixed results. *Moringa Oleifera*, a plant also known as the tree of life or miracle tree, belongs to the genus *Moringaceae*, which is native to the tropics and sub-Himalayan areas of India, Pakistan, Bangladesh, and Afghanistan. The immature green pods, also known as drumstick, are consumed in different ways, such as cooking the pods (as with green beans) or preparing the leaves like spinach. Along with the glycemic control in diabetes, *M. oleifera* has other medicinal purposes: asthma, hyperlipidemia, hypertension, hormone disorders, and gastrointestinal disorders. Based on human studies, the plant has been proposed to decrease glucose levels by increasing insulin secretion and sensitivity and by inhibiting amylase and glucosidase activities. Proven by some animal studies, additional proposed mechanisms of action include increased glucose uptake in the muscle and liver, inhibition of glucose uptake in the intestine, and decreased gluconeogenesis in the liver. ⁽⁵⁾

The leaves are also widely used as vegetable, condiment and in salads. *M. Oleifera* leaves are non-toxic. This has been confirmed by laboratory experiments such as: The aqueous extract of *M. Oleifera* leaves was administered orally to 30 male Wistar rats and even in doses of 2000 mg/kg no mortality ensued. Sub-acute toxicity was assessed by administering daily doses of up

to 1600 mg kg to male rats, and no signs of serious toxicity were observed on biochemical or haematological tests, or on histopathology of the organs. The safety of M.Oleifera leaves has been confirmed in other studies ⁽⁶⁾

In different studies, different dosage of M. Oleifera leaf powder capsules have been used. Ten healthy volunteers were enrolled in this study, after an overnight fast and every two weeks, subjects received an oral dose of MO at increasing dosages of 0, 1, 2, and 4 g. Plasma glucose (PG) and insulin were collected at baseline and at 0.5, 1, 1.5, 2, 4, and 6 hours after each MO dosage administration and it was scientifically proven that the widely claimed use of M. oleifera as an ethno-medicine is useful in treating diabetes mellitus. ⁽⁷⁾

A few human studies are reported on the use of Moringa Oleifera, most of trials are reported on animals. In Pakistan no such study is available but people in the rural parts do take it as a myth to treat different diseases.

Rationale:

Since the studies have shown the effect of Moringa leaves on lowering the blood glucose levels in animals and diabetic patients, however, the sufficient investigation has not been done on human on large scale to check the effect and their use as an alternative treatment option for diabetic patients. Thus, this study is being conducted to assess the effect of Moringa leaf on Diabetics' Glycemic Control.

Objectives:

- To assess the combined effect of metformin and Moringa leaf capsules on glycemic control of Type 2 diabetic patients.
- To assess the safety of Moringa leaf capsules in Type-2 Diabetic Patients.
- To study its effects on blood pressure, BMI, and creatinine levels.

Hypothesis:

Moringa Leaf capsules shows positive outcome in lowering the blood glucose levels and is safe for Type 2 Diabetic patients.

Null Hypothesis:

Moringa Leaf capsules does not have any effect on blood glucose levels and is not safe for Type 2 Diabetic patients

Operational Definition:

Type 2 diabetes: It is characterized by increased fasting plasma glucose ≥ 126 mg/dL (7.0 mmol/L), and HbA1C $\geq 6.5\%$ (48 mmol/mol) for many nonpregnant adults. ⁽⁸⁾

Glycemic Control: HbA1c level of $\geq 7.0\%$ will be considered as 'poor glycemic control'. ⁽⁹⁾

Type 2 Diabetic Patients will be divided into two groups based on their HbA1c levels:

Group A: All the patients with HbA1c $< 7.0\%$

Group B: All the patients with HBA1c > 7.0%.

Methodology:

A randomized controlled trial will be conducted in Akber Niazi Teaching Hospital ANTH.

Study Duration:

01 year

Sample size:

Confidence interval: 95%

Ratio of sample size: 1

Power: 80%

Mean and Standard Deviation of group 1: 10.07±2.07

Mean and Standard Deviation of group 2: 8.79±0.10

Sample size: 42

As this study is expected for 3 months and the dropout of 20% IS being expected; Therefore, Total sample size has been increased to 50.

Total Sample Size: 50

Exclusion criteria:

- Patients having Type I diabetes
- Pregnant women
- The patients with deranged LFTs and RFTs.
- Patients having Creatinine levels more than 1.2 mg/dl in man and >1.1mg/dl in female.⁽¹⁰⁾
- Patients of Type II diabetes on insulin therapy

Inclusion criteria:

- The patients having type 2 diabetes.
- The patients who willingly consent.

Sampling Technique:

- Random sampling technique will be used to collect the data from type 2 diabetic patients.
- Written informed consent will be taken before any examination.
- Only the researchers will have the excess to the patients', and it will be kept confidential.
- Pilot testing will be done on 5% of the sample before conducting the whole study.

Procedure:

1. A questionnaire consists of diabetic history, demographics, and Anthropometric measure will be used for the study.

2. The questions regarding any side effects will be included in the questionnaire.

3. Glycated hemoglobin (HbA1c) will be determined by high-performance liquid chromatography.

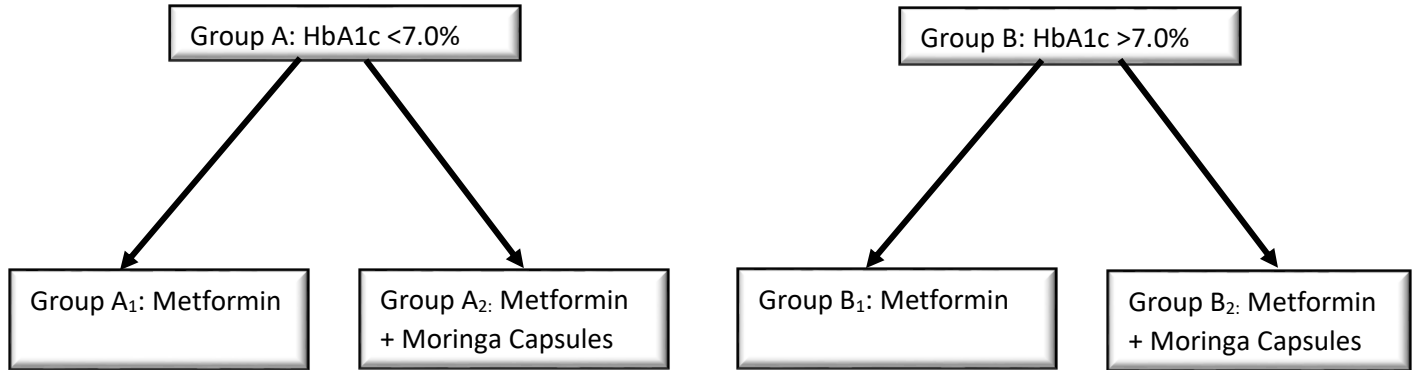
4. The patients will be divided into two groups:

Group A: Having HbA1c <7.0%

Group B: Patients Having HbA1c >7.0%

Group A will be further divided into two subgroups, one group will be given metformin and the other one will be given Metformin plus Moringa leaf Capsules.

Similarly, Group B will also be further divided into Two groups, half of the patients will be given metformin and the other half will be given metformin plus Moringa leaf Capsules.



5. 1g Capsules will be used for the study for 3-month duration in type 2 Diabetic patients. ⁽¹¹⁾

6. Fasting Blood glucose levels and HbA1c levels, LFTs, RFTs and lipid profile will be checked thrice, before starting the treatment, after ½ month, and at the end of treatment.

7. To assess the safety of capsules the Lipid function test(LFTs), renal function test(RFTs), and lipid profile will be performed. If any value is deranged, the patients will be included in the study.

Statistical Analysis:

SPSS version 26 will be used for the analysis. The Continuous variables will be expressed in the mean ± SD or median (min, max). Frequencies and percentage will be used for the categorical

variables. Finally, Paired T test and One way Anova will be applied to compare before and after treatment effects. For analysis, P value < 0.05 will be considered significant.

Ethical consideration:

- The response forms will be accessible to the study participants only. Thus, their information will be kept strictly confidential.
- Sample of informed consent provided in Annexure B.
- No mentionable risks are involved in this study.

Significance:

- Diabetes is a lifelong disease and researchers are striving to come up with affordable options to control diabetes. Thus, this study will help us find an economical way of controlling the Type 2 Diabetes.
- No Side effects of Moringa has been reported to date in any study conducted on animals and humans.

Conflict of interest: There is no conflict of interest to report.

References:

- (1) Azeem S, Khan U, Liaquat A. The increasing rate of diabetes in Pakistan: A silent killer. *Annals of Medicine and Surgery*. 2022 Jul;79.
- (2) Gillani AH, Aziz MM, Masood I, Saqib A, Yang C, Chang J, Mohamed Ibrahim MI, Fang Y. Direct and indirect cost of diabetes care among patients with type 2 diabetes in private clinics: a multicenter study in Punjab, Pakistan. *Expert review of pharmacoeconomics & outcomes research*. 2018 Nov 2;18(6):647-53.

- (3) Owens III FS, Dada O, Cyrus JW, Adedoyin OO, Adunlin G. The effects of Moringa oleifera on blood glucose levels: a scoping review of the literature. *Complementary Therapies in Medicine*. 2020 May 1;50:102362.
- (4) Kumar PK, Mandapaka RT. Effect of moringa oleifera on blood glucose, ldl levels in types ii diabetic obese people. *Innov. J. Med. Health Sci*. 2013;3:23-5.
- (5) Haber SL, McMahon RP, Barajas J, Hayes AR, Hussein H. Effects of Moringa oleifera in patients with type 2 diabetes. *American Journal of Health-System Pharmacy*. 2020 Oct 30;77(22):1834-7.
- (6) Sissoko L, Diarra N, Nientao I, Stuart B, Togola A, Diallo D, Willcox M. Moringa oleifera leaf powder for type 2 diabetes: a pilot clinical trial. *African Journal of Traditional, Complementary and Alternative Medicines*. 2020 Nov 18;17(2):29-36.
- (7) Anthanont P, Lumlerdkij N, Akarasereenont P, Vannasaeng S, Sriwijitkamol A. Moringa oleifera leaf increases insulin secretion after single dose administration: a preliminary study in healthy subjects. *J. Med. Assoc. Thail*. 2016 Mar 1;99:308-13.
- (8) American Diabetes Association. 2. Classification and diagnosis of diabetes: standards of medical care in diabetes—2021. *Diabetes care*. 2021 Jan 1;44(Supplement 1):S15-33.
- (9) Omar SM, Musa IR, Osman OE, Adam IJBrn. Assessment of glycemic control in type 2 diabetes in the Eastern Sudan. 2018;11(1):1-5.
- (10) Shahbaz H, Gupta M. Creatinine clearance.
- (11) Sissoko L, Diarra N, Nientao I, Stuart B, Togola A, Diallo D, Willcox M. Moringa oleifera leaf powder for type 2 diabetes: a pilot clinical trial. *African Journal of Traditional, Complementary and Alternative Medicines*. 2020 Nov 18;17(2):29-36.

ANEXURE A:

Effect of Moringa leaf capsules on glycaemic control of Type 2 diabetic patients: A Randomized Controlled trial.

General Information

Name: _____ MR No _____

Age: _____

Sex: Male Female Other

Date of birth: _____ Phone number: _____

Address: _____

City: _____ Ethnicity: _____

Marital status: Married Unmarried other Diabetic: Type 1 Type 2

Height: _____ Weight: _____ HbA1c levels: _____

When were you first diagnosed with Diabetes?
Year: _____ Age: _____

Medication

1. Do you take any medications/pills for your Diabetes? Yes No

If yes, please specify the amount and frequency: _____

2. Are you allergic to any homeopathic medicine? Yes No

3. Have you ever used the Moringa leaves to control diabetes? Yes No

Before supplementation:

HbA1c: _____ Fasting Blood Glucose levels: _____

Systolic Blood Pressure: _____ Diastolic Blood Pressure: _____

Creatinine levels: _____ LFTs: _____

RFTs: _____

After ½ month:

HbA1c: _____

Systolic Blood Pressure: _____

Creatinine levels: _____

RFTS: _____

At the End of Study:

HbA1c: _____

Systolic Blood Pressure: _____

Creatinine levels: _____

RFTS: _____

Fasting Blood Glucose levels: _____

Diastolic Blood Pressure: _____

LFTs: _____

Fasting Blood Glucose levels: _____

Diastolic Blood Pressure: _____

LFTs: _____

ANNEXURE B:

Informed Consent form for participation in research 'Effect of Moringa leaf capsules on glyemic control of Type 2 diabetic patients: A Randomized Controlled trial'

I _____ confirm that I have read and understood the information shared with me regarding
the aforementioned topic.

I understand that my participation is voluntary and I am free to withdraw at any time without giving any
reason, without my medical and legal rights being affected.

I am aware that my information will be kept confidential.

I agree to take part in the project which will include being interviewed and recorded.

I have been informed regarding the potential risks that could happen during the study.

Patient's name: _____

Patient's signature _____

Researcher's name _____

Researcher's signature _____

