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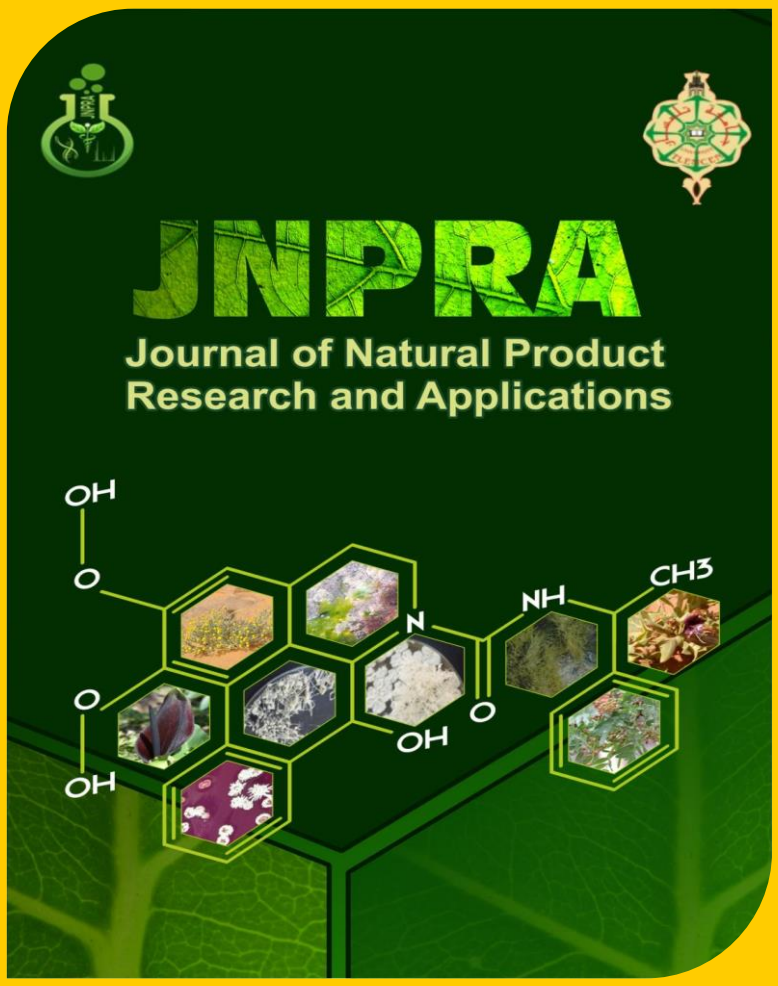

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Research Article

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Comparative study of serum biochemical parameters between diabetic patients using medicinal plants and those using only conventional treatment in the rural region of the province of Tlemcen (North-western Algeria)

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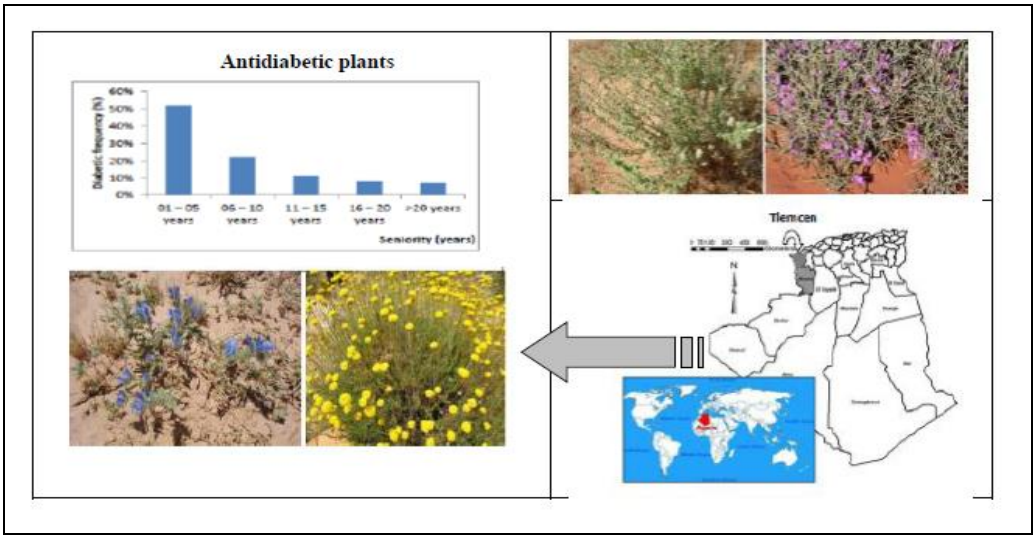
Highlights

- 148 diabetic patients from Fellaoucene rural region respond to the questionnaire.
- 21% of diabetics use medicinal plants to manage or to treat their diabetes.
- 39 medicinal plants, from 21 families, are listed in our survey;

Graphical Abstract



Abstract
A survey is carried out on 148 diabetic patients from rural Fellaoucene, Tlemcen Province (North-Western Algeria).
The main interest of this study is to determine the frequency of diabetic patients using medicinal plants with their conventional medication to relieve their diabetes mellitus and to compare their serum biochemical parameters with patients do not use these plants in combination with drugs.
A questionnaire is used to collect information about patients (age, sex), diabetes (duration, type, treatments, and complications), antidiabetic plants use (vernacular, scientific names) and variation of some serum biochemical parameters (glycemia, triglyceride, cholesterol, urea, creatinine, glycated hemoglobin (HbA1c)).
72% of diabetic patients are type 2 diabetes mellitus and 77% of them are women with a mean age of 53 years. More than 26% of the cases are suffering from diabetes for more than 10 years. 96% of the patients are affected by at least one chronic complication. The results show that 21% of diabetics use medicinal plants without any significant effects on the balance of the biochemical parameters tested. We notice a slight increase in glycemia (1.39±0.48 g/l) and HbA1c (7.27±0.69 %) of both populations when compared to the values recommended by WHO (1.26 g/l and 6.5%, respectively).
The medicinal plants still have a place in the treatment of diabetes mellitus in the rural region of Fellaoucene, Tlemcen (Algeria)

Keywords: Diabetes mellitus; Survey; Northwestern Algeria; Biochemical parameters; Antidiabetic plants.

1. Introduction

Diabetes mellitus, especially type 2 (T2DM), has been considered worldwide in recent years as one of the scourges of the third millennium in developed and developing countries. The number of people with diabetes continues to grow dramatically in the last 30 years. It was estimated that in 2017 there are 451 million (age 18–99 years) people with diabetes worldwide. These figures were expected to increase to 693 million by 2045 (Cho et al., 2018). According to the Algerian Federation of Diabetic Associations (AFDA), 5 million of Algerians are suffering from diabetes because of several factors such as stress, obesity, sedentary, lifestyle ... (AFDA, 2016). Diabetes is a heterogeneous group of metabolic diseases which main characteristic is hyperglycemia resulting from defects in insulin secretion, insulin action, or both (WHO, 2002). The current treatment of type 2 diabetes is used to help to manage the disease. Till now there is no cure. Its treatment is based on improving the sensitivity to insulin action by regular physical activity, dietary measures and medication insulin sensitizers. It is also based on increasing insulin's secretion by means of insulin-secreting drugs (Charbonnel and Cariou, 1997). However, these different therapeutic approaches remain ineffective for a number of diabetics. This is due to the chronicity of the disease, the socioeconomic level (lower purchasing power), poor access to medical facility

and the unavailability of antidiabetic drugs. Most diabetics in Algeria, as well as in other developing and undeveloped countries, show a great growing interest in alternative treatments with medicinal plants. Ethnobotanical data collected in several parts from the world indicate the use of more than 1123 plant species for their hypoglycemic and antihyperglycaemic properties (Bailey and Day 1989, Marles and Farnsworth 1995, Eddouks et al. al., 2007, Azzi et al., 2012). The purpose of this study is to carry out a descriptive survey on diabetics in Fellaoucene rural region, Tlemcen (Algeria). It concerns to analyze some of their serum biochemical parameters and to compare between diabetic patients using medicinal plants, in order to improve their health condition, and those using only conventional treatment prescribed by doctors.

2. Materials and Methods

2.1. Study area

A survey is conducted using a questionnaire to identify antidiabetic plants used by the diabetic population in the region of Fellaoucene, Tlemcen Province (North-Western Algeria), during February and March 2018. This rural region "Fellaoucene" is located in the northern part of Tlemcen province (Algeria). It has a population of approximately 9.300 inhabitants (ONS Algeria, 2008). It features a semi-arid climate characterized by hot dry summers and mild, wet winters. A number of 148 diabetic patients (type 1/ type 2) are addressed a questionnaire to fulfill informing them about the objective of the study.

2.2. Questionnaire

The questionnaire includes four parts to gather information about the patients (first name, age and sex), the disease (age of diabetes, type of diabetes, treatment and complications), questions related to the use of presumed antidiabetic plants (frequency of use of plants, vernacular and scientific names) and the evolution of some biochemical parameters (glycemia, total cholesterol, triglyceride, urea, creatinine, HbA1c).

Inclusion criteria: diabetics admitted to Public Health Establishment of Proximity of Fellaoucene during the months of February and March 2018.

Exclusion Criteria: non-diabetic subjects do not have any inclusion criteria.

2.3. Assays for serum biochemical parameters

Participants are selected for the biochemical parameter assays (glycemia, total cholesterol, urea, creatinine, triglyceride, HbA1c). The assays are carried out in analysis laboratory of Public Health Establishment of Proximity of Fellaoucene. The determination of blood glucose, triglyceride and cholesterol levels is performed by enzymatic assays according to the methods described by Trinder (1969), Fossati and Prencipe (1982) and Fasce (1982), respectively. Serum creatinine is determined within an alkaline solution according to Jaffé method (Murray et al., 1984) while serum urea assay is performed by a colorimetric enzymatic technique supplemented with a colored chemical reaction (Mac Key et Rackeyll,

1927). Glycated hemoglobin (HbA1c) is measured by High-Performance Liquid Chromatography method (HPLC) which separates HbA1c and non-glycated hemoglobin according to their different electrical quantities. The stationary phase is a weak acid cation-exchange phase. The elution of the separated HbA1c passes through UV light of 415 nm. Absorbances give a corresponding hemoglobin chromatogram. HbA1c is indicated by the percentage of HbA1c peak in the total hemoglobin area.

3. Results

3.1. Distribution of diabetics by gender and age

A number of 148 diabetic patients from Fellaoucene rural region respond to the proposed questionnaire. 39 among the participants are type 1 diabetes, 106 of them are type 2 diabetes whereas 3 cases have gestational diabetes. The collected data demonstrate that diabetes is more frequent in women (114 cases, 77%) than in men (34 cases, 23%) with a ratio of 3.35.

The median age of the study population is 53 years, ranging from 18 to 92 years. It has been observed that the frequency of diabetics increases with age. The most affected group is between 46 and 60 years (43%) (Figure 1). This number decreases significantly after the age of 75 (only 10%).

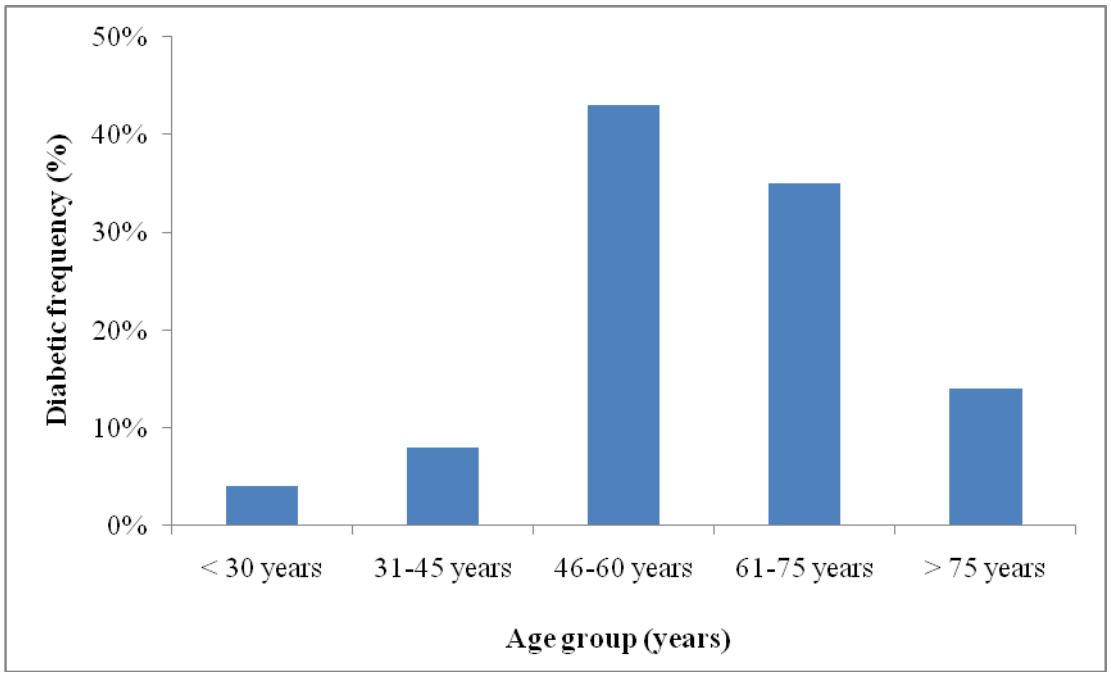


Figure 1. Distribution of diabetics by age.

3.2. Clinical status of diabetic subjects

According to the gathered results, type 2 diabetes is more prominent (72%) than type 1 diabetes (26%). Hence gestational diabetes presents the least percentage of 02%. Results show that 26% of the respondents are suffering from diabetes for more than 10 years (with 10 cases over than 20 years of suffering). Thus, the majority of them (74%) have the disease for less than 10 years (Figure 2).

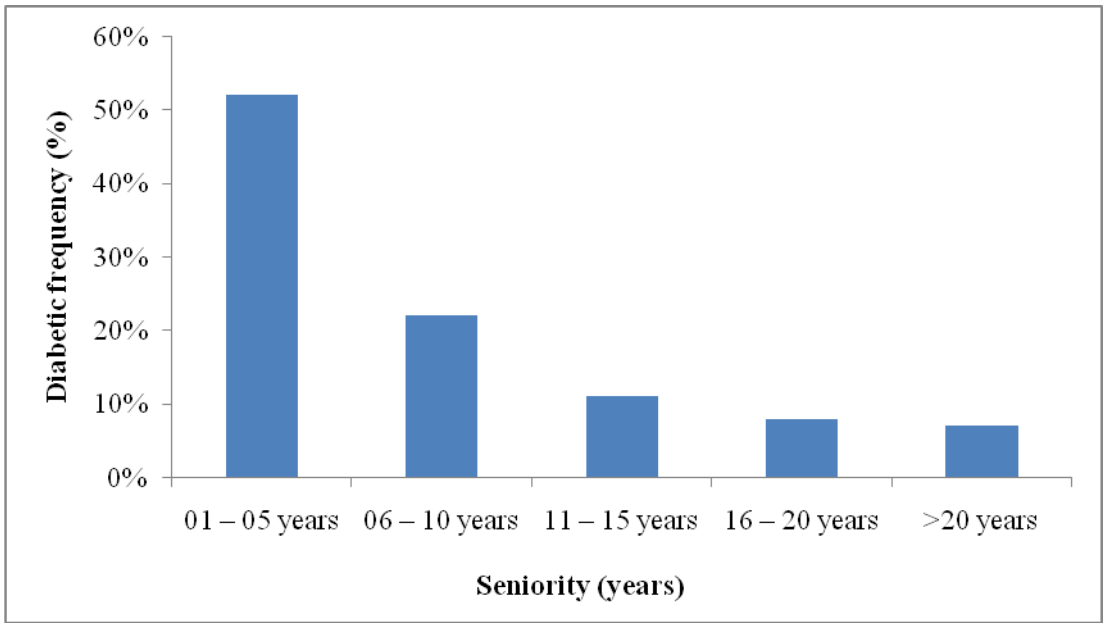


Figure 2. Distribution of diabetics by age of diabetes.

Among diabetics, only 79 of them follow diet restrictions to manage their diabetes. The total number of diabetics type 1 take insulin as a single treatment. Whereas, the majority of type 2 diabetics are treated with oral antidiabetic drugs either with hypoglycemic sulfonamides or biguanides or both. In addition, it has been recorded that 03% of type 2 diabetics use insulin therapy in combination with oral anti-diabetics drugs (Figure 3).

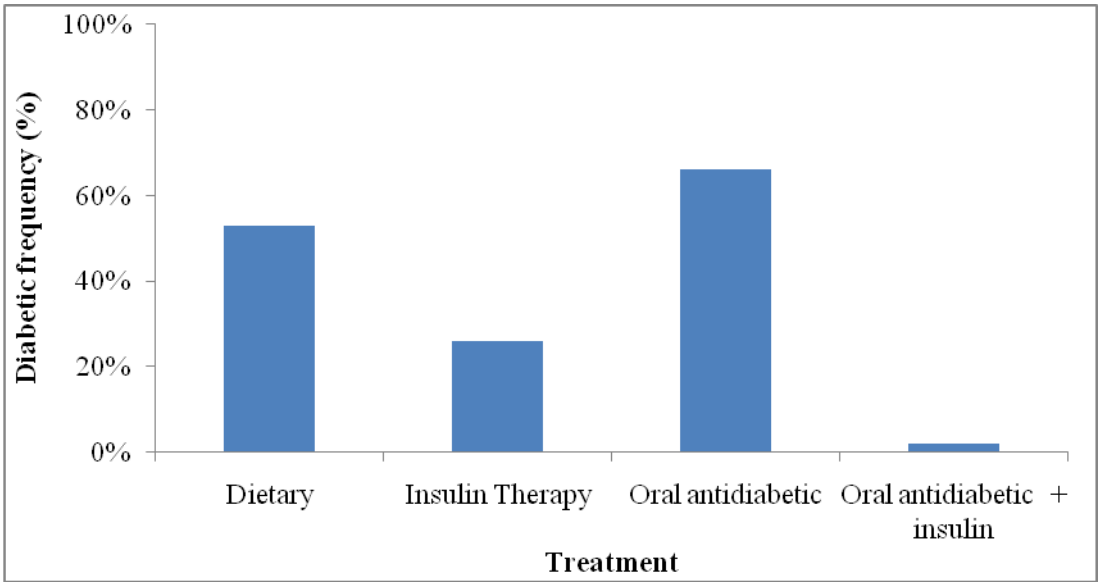


Figure 3. Distribution of diabetics according to their treatment.

In this study, it has been found that more than 96% of the participants suffer from at least one chronic complication either microangiopathic (vision or kidney disorders) or macroangiopathic (heart disorders, arterial hypertension). It is noticed that 99 of the cases

have vision disorder and 96 of them have arterial hypertension. A number of 17is recorded for cardiac disorders diabetics and 11 patients with renal disorder complication (Figure 4). Moreover, 4% of diabetics have no complication. They are affected by diabetes for less than 10 years.

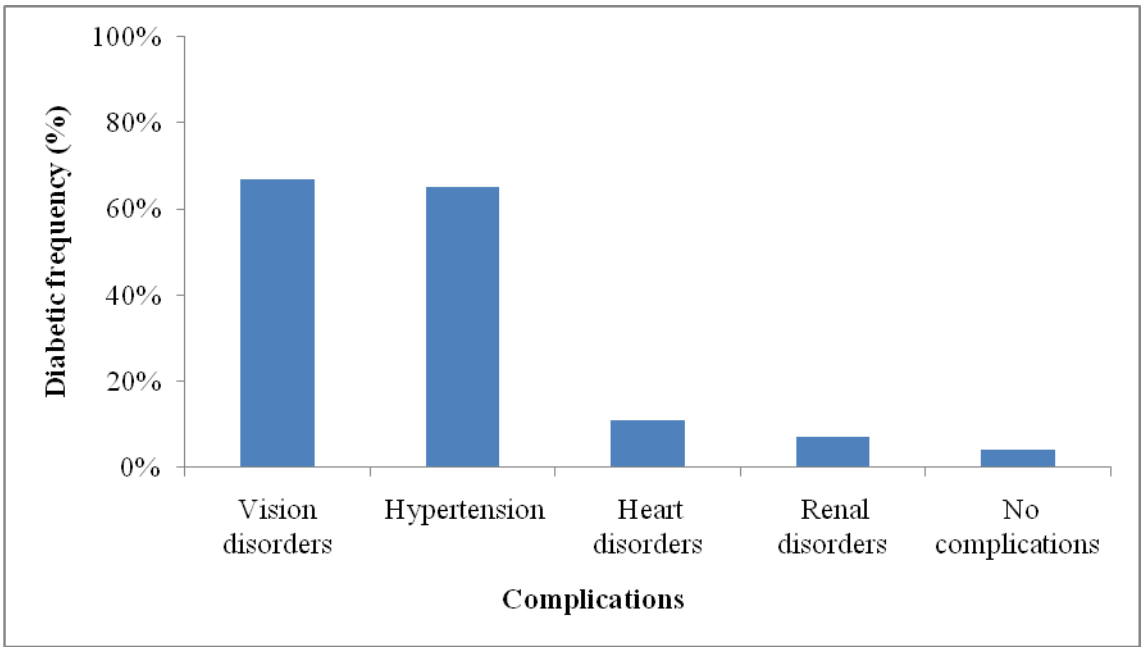


Figure 4. Distribution of diabetics according to their health complications.

3.3. Use of antidiabetic plants

The ethnopharmacological study, conducted in rural area of Fellaoucene, demonstrate the frequency of participants in using medicinal plants for the treatment of their diabetes mellitus. **Table 1** gathers the responses of patients: whether they use plants or not, their knowledge about antidiabetic plants and the efficacy of these plants used to relieve their diabetes.

Table 1. The importance of use of antidiabetic plants by the population surveyed

Participants	Number	% of total Diabetics
Diabetics use plants	32	21%
Diabetics do not use plants	116	79%
Diabetics know the plants	33	22%
Diabetics do not know plants	115	78%
Diabetics judge plants effective	32	21%
Diabetics judge plants ineffective	116	79%

A minor percentage of 21% (32) of participants knows about medicinal plants and uses them (at least one) in their treatment of diabetes. They use only plants or plants in combination with their conventional drugs of diabetes mellitus. While more than 79% of them ignore the effectiveness of medicinal plants (Table 1). Of 76 citations, 38 medicinal plants (from 21

families) are listed and classified in number of citations. 21 plants are cited only once whereas 08 plants are scored more than 02 citations. These plants are: Oregano leaves (*Origanum compactum Benth* : 07 citations), Olive leaves (*Oleaeuropaea L.*: 06 citations), Pomegranate pericarp (*Punicagranatum L.*: 05 citations), Almond seeds (*Prunusdulcis(Mill.) D.A.Webb*.: 04 citations), the aerial part of False Parsley (*Ammoidespusilla (Brot.) Breistr.*: 04 citations), Leaves of Loquat (*Eriobotryajaponica (Thunb.) Lindl.*: 03 citations), leaves of Calphe nepeta (*Calamintha nepeta*: 03 citations), leaves of Myrtle (*Myrtuscommunis* L.: 03 citations).

3.4. Biochemical parameters alteration

Table 2 summarizes results of the alteration of some serum biochemical parameters of diabetics use medicinal plants in their treatment and patients who use only conventional drugs: glycemia, HbA1c, total cholesterol, triglycerides, urea and creatinine.

Table 2. Variation of some serum parameters of participants according to their use of medicinal plants.

Serum parameters	Usuel value	Mean ± SD	
		Diabetics use medicinal plants (n = 32)	Diabetics do not use medicinal plants (n = 116)
Glycemia **(g/l)**	1.10 – 1,26	1.31 ± 0.37	1.39 ± 0.48
Total Cholesterol **(g/l)**	≤ 2	1.68 ± 0,47	1.67 ± 0.45
Triglycerides **(g/l)**	≤ 2	1.40 ± 0,70	1.64 ± 0.39
Urea **(g/l)**	0.18 – 0.45	0.26 ± 0,07*	0.34 ± 0.03
Creatinine **(mg/l)**	9 – 12	8.07 ± 0,59	8.76 ± 1.25
HbA1c **(%)**	4.5 – 6.5	7.27 ± 0,69	6.70 ± 1,21

*insignificant (P <0.05)

According to the results obtained, no significant difference is recorded between biochemical parameters of diabetics using medicinal plants with their drugs and the other patients using only conventional medication. A slight significant decrease of serum urea ($P < 0.05$) is noticed for diabetics using medicinal plants in comparison with diabetics do not use these plants. Compared to the standards, glycemia and HbA1c reveal a slight increase in both populations while all the other parameters are normal (Table 2).

4. Discussion

In the current research, a questionnaire is used to collect information from a diabetic population from rural region of Tlemcen Province (North-Western Algeria). The main objective is to have an overview on the antidiabetic medicinal plants and their effectiveness comparing between serum biochemical parameters (glycemia, triglycerides, cholsterol, urea, creatinine and HbA1c) of a population who uses plants and another one takes only ordinary

diabetes medication. Among148 participants, 72% of the cases are type 2 diabetics and 77% of them are women. The average age of this population is 53years whereas the maximum proportion is from age group 46-60 years (43%). More than 26% of the cases have diabetes for more than 10 years and most of them (over 96%) suffer from at least one chronic complication. These results are similar to those reported in literature in various epidemiological studies on diabetes mellitus in the Algerian population. In a survey conducted by Azzi et al. (2012) on 470 diabetics from four Provinces in northwestern and southwestern of Algeria, 59.15% of diabetics are type 2 diabetics and 57.87% of them are women. The average age of this population is 53 years while more than 52% of the cases have diabetes for more than 10 years (Azzi et al., 2012). The National Health Survey, published in June 2005 by the National Institute of Public Health in Algeria, estimate a prevalence of 12.3% of diabetics among 4818 people aged from 35 to 70 without a significant difference noticed by sex (11.9% for men and 12.5% for women). Hence, type 2 diabetes is detected more frequent in age group 65- 70 years (22.37%) (TAHINA,2007). Another study, conducted in the region of Tlemcen (Western Algeria) on a sample of 7 656 people aged over 20 years, demonstrates different results. The estimated prevalence of diabetes is 14.2% which is nearly doubled for men than for women (20.4% versus 10.7%). Moreover, this prevalence is revealed higher in urban areas (15.3%) than in rural ones (12.9%). Similarly, 60% of diabetics have at least one degenerative complication (Zaoui et al., 2007). In Algeria, the search for hypoglycemic plants has known a prominent appearance in recent years through ethnopharmacological surveys. Algeria is known by its biodiversity, its geographical situation and its climate which enhance the knowledge of inhabitants about herbal medicine treating chronic diseases and diabetes mellitus in particular especially in rural areas. In the present study, a proportion of 21% of diabetics use medicinal plants to manage or to treat their diabetes. This low percentage may be explained by the good management of diabetics (by health structures and associations), the improvement of their socioeconomic level or/and their awareness. In addition, we may suggest that the lack of respect of some rules in handling plants such as doses, inadequate conditions of conservation of plants, time and mode of preparation increases the risk of poisoning and the appearance of side effects in diabetics. This may alter some serum biochemical parameters (carbohydrate and lipid) and disrupt the function of liver and kidney organs. Furthermore, type 1 diabetics use less medicinal plants than type 2 diabetics with percentages of 13% and 25%, respectively. This difference is due to the risk of hypoglycemic accidents that mainly affect patients with type 1 diabetes. These findings are low compared to those mentioned in literature.

Ethnobotanical studies carried out by Azzi et al. (2012) and Allali et al. (2008) demonstrate proportions of 28.30% and 62% on the employ of medicinal plants by the western population of Algeria, respectively . In similar, other studies carried out in different regions in Morocco indicate the significant dependence of the local population on medicinal plants in dealing with diabetes (Ziyyat et al., 1997; Jouad et al., 2001; Eddouks et al., 2002; Tahraoui et al., 2007). A number of 39 medicinal plants, from 21 families, are listed in our survey. It is noticed that 08 plants are cited more than 2 times. Their popularity may attribute to tradition,

efficiency, availability and/or low cost. Some cited plants are common with other traditional pharmacopoeia, especially those from the Mediterranean. Cultural mixture promotes the exchange of know-how on traditional care systems. Dietary habits and nutritional factors are considered important in dietetics, the treatment and the prevention of diabetes mellitus. Thus, Algerian cooking is characterized by its diversity and richness in plant species (vegetables, spices, fruits) used for food ingredients and for their therapeutic properties. Bnouham et al. (2006) summarize in a bibliographical synthesis all the antidiabetic plants studied and reported in literature between the years of 1990 and 2000. They have identified 176 plant species integrated into 84 families with clear antidiabetic power.

Analysis of serum parameters (glycemia, HbA1c, total cholesterol, triglyceride, urea and creatinine) does not reveal any significant difference between diabetics take medicinal plants as treatment and others use only their conventional drugs. This is probably due to the effectiveness of conventional medication for diabetics although the slight increase of their glycemia (1.39±0.48 g/l) and HbA1c (7.27±0.69%) in comparison with the standards recommended by WHO (World Health Organization) and ADA (American Diabetes Association) (Alberti and Zimmet, 1998; ADA, 2016).These results are comparable with the average results of HbA1c (8.71% in women and 8.37% in men) in a diabetic population in the western region of Algeria (Rahmoun et al., 2018; Rahmoun et al., 2019).

5. Conclusions

In light of the results obtained in this study, we conclude that medicinal plants still have a place in the treatment of diabetes mellitus in the rural region of Fellaoucene, Tlemcen (Algeria). A frequency of 21% of diabetics uses phytotherapy. It has been shown that the antidiabetic plants used do not affect the balance of the analyzed biochemical parameters. This use of antidiabetic plants must be based on the results of the well-conduct of scientific studies when specifying the mechanism of action of the plant, the therapeutic and the toxic dose. Thus, medicinal plants represent a certain potential source of hypoglycemic substances that have also their toxicological side effects which can be fatal in some cases. That is why, the need for continuous vigilance is still recommended.

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Author Contribution Statement

Azzi Rachid supervised the findings of this work; Dounia MEZOUAR, Fayza ABBOU, Souad MAHDI: Carried out the survey; Nacéra BELKACEM, Nabila BENARIBA, Farid Boucif LAHFA: discussed the results and contributed to the final manuscript.

Conflict of interest

Authors declare no conflict of interest.

References

ADA: American Diabetes Association. 2016. Diabetes Classification and Diagnosis of Diabetes. *Diabetes Care*, 39 (Suppl.1): 513-522.

AFDA : Algerian Federation of Diabetic Associations. 2016. Journée nationale des diabétiques. Relizene.

Alberti, K.G., Zimmet, P.J. 1998. Definition and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus provisional report of a WHO Consultation. *Diabet. Med*, 15 (7): 539-553.

Allali, H., Benmehdi, H. , Dib, M.A., Tabti, B., Ghalem, S., Benabadji, N. 2008. Phytotherapy of Diabetes in West Algeria. *Asian journal of chemistry*, 20 (04): 2701-2710.

Azzi, R., Djaziri, R., Lahfa, F., Sekkal, F.Z., Benmehdi, H., Belkacem, N. 2012. Ethnopharmacological survey of medicinal plants used in the traditional treatment of diabetes mellitus in the North Western and South Western Algeria. *J. Med. Plants Res*, 6(10): 2041-2050.

Bailey, C.J., Day C. 1989. Traditional plant medicines as treatment for diabetes. *Diabetes Care*; 12: 553-564.

Bnouham, M., Ziyyat, A., Mekhfi, H., Tahri, A., Legssyer, A. 2006. Medicinal plants with potential antidiabetic activity – A review of ten years of herbal medicine research (1990-2000). *Int. J. Diabetes Metab*, 14: 1-25.

Charbonnel, B., Cariou, B. 1997. Diabète non insulinodépendant: indications thérapeutiques. *Médecine thérapeutique* ; 3.hs: 103-11.

Cho, N.H., Shaw, J.E., Karuranga, S., Huang, Y., Da Rocha Fernandes, J.D., Ohlrogge A.W., Malanda B. 2018. IDF Diabetes Atlas: Global estimates of diabetes prevalence for 2017 and projections for 2045. *Diabetes Res. Clin. Pract*, 138: 271-281.

Eddouks, M., Maghrani, M., Lemhadri, A., Ouahidi, M.L., Jouad, H. 2002. Ethnopharmacological survey of medicinal plants used for the treatment of diabetes mellitus, hypertension and cardiac diseases in the south-east region of Morocco (Tafilalet). *J. Ethnopharmacol*, 82: 97-103.

Eddouks, M., Ouahidi, M.L., Farid, O., Moufid, A., Khalidi, A., Lemhadri, A. 2007. L'utilisation des plantes médicinales dans le traitement du diabète au Maroc. *Phytothérapie*, 5: 194-203.

Fasce, C.F. 1982. Serum Cholesterol determined colorimetrically with enzyme. *Clin. Chem*; 18: 901.

Fossati, P., Prencipe, L. 1982. Serum triglycerides determined colorimetrically with an enzyme that produces hydrogen peroxide. *Clin. Chem*, 28: 2077-2080.

Jouad, H.M., Haloui, M.H., Rhiouani, H., El Hilaly, J.M., Eddouks, M. 2001. Ethnobotanical survey of medicinal plants used for the treatment of diabetes, cardiac and renal diseases in the North centre region of Morocco (Fez–Boulemane). *J. Ethnopharmacol*, 77: 175-182.

Mac Key, E.M., Rackeyll, J. 1927. *Clin.invest J*, 4: 295.

Marles, R.J., Farnsworth N.R. 1995. Antidiabetic plants and their active constituents. *Phytomedicine*, 2: 13-189.

Murray, R.L. 1984. Creatinine In: Clinical Chemistry; Theory, Analysis and Correlation, Kaplan, L.A., Pesce A.J. (Ed.) CV Mosby Company St Louis: 1247-1253.

ONS Algeria, 2008. National Statistical Office Algeria, General Census of Population and Housing 2008: Preliminary results of the 2008 population census. Accessed on 2008-07-02.

Rahmoun, M.N., Ghembaza, A., Habi, M.A. 2018. Glycated hemoglobin assay in a Tlemcen population: Retrospective study. *Diabetes Metab Syndr*, 12(6): 911-916.

Rahmoun, M.N., Ghembaza, C.E., Ghembaza, M. E. A. 2019. Lipid profile in type 2 patients with diabetes from Tlemcen: A Western Algerian population. *Diabetes Metab Syndr*, 13(2): 1347-1351.

TAHINA: Epidemiological Transition and Health Impact in North Africa, INSP: National Institute of Public Health in Algeria. 2007. The National Health Survey 2005: Epidemiological transition and health system Project TAHINA, Algeria. ; Contrat n° ICA3-CT-2002-10011).

Tahraoui, A., El-Hilally, J., Israili, Z.H., Lyoussi, B. 2007. Ethnopharmacological survey of plants used in the traditional treatment of hypertension and diabetes in South-eastern Morrocco. *J. Ethnopharmacol*, 110: 105-117.

Trinder, P. 1969. Determination of glucose in blood using glucose oxidase with an alternative oxygen receptor. *Ann Clin. Biochem*, 6 : 24 - 27.

WHO : World Health Organization. Diabète sucré. 2002. Aide mémoire. ; N°138.

Zaoui, S., Biemont, C., Meguenni, G. 2007. Epidemiology of diabetes in urban and rural regions of Tlemcen (Western Algeria)]. *Santé*, 17:15-21.

Ziyyat, A., Legssyer, A., Mekhfi, H., Dassouli, A., Serhrouchni, M., Benjelloun, W. 1997. Phytotherapy of hypertension and diabetes in oriental Morocco. *J. Ethnopharmacol*, 58: 45-54.