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Perception of Patient Population on Use of Medications in Type 2 Diabetes Mellitus and Awareness of Occurrence of Herb Drug Interaction

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ABSTRACT
Diabetes is the most common metabolic disorder. Modern therapy has numerous side effects, is expensive and is unable to effectively control the metabolic defects of the disease and their consequences. The traditional medicinal plant extracts or different folk plant preparations have been used by physicians and laymen to treat diabetes since decades. Herbal medicines affect pharmacokinetics and pharmacodynamics properties of drugs leading to Herb-Drug interactions. The aim of this survey was to assess the level of awareness and perception towards herbs as complementary medicine and HDI. Survey was carried out in diabetic patients using the designed health survey sheet. It was observed that the majority of respondents were undertaking combination therapy of allopathic drug with herbal/ayurvedic medicines, of which an alarming number 90 % had not reported the same to their physicians. Also patients were not aware of the possibility of occurrence of HD interactions. This survey throws light on the need to educate both the physicians and the patients on HDI interactions, which needs to be strictly monitored as it may cause serious complications. Hence, proper reporting of cases, careful vigilance, and constantly updated reviews of HDI is essential to update physicians' practices, additional training and integration of knowledge and expertise to improve the therapeutic efficacy, drug compliance and safety of patients.
Key words: Diabetes mellitus; Health survey; Herb drug interaction; Pharmacokinetics; Pharmacodynamics

INTRODUCTION

There are an estimated 382 million people with diabetes are aged between 40 and 59, and 80% of them live in low- and middle-income countries., according to the International Diabetes Federation (IDF), and this figure is set to rise 55%by 2035.[1] Every year, 7 million people worldwide develop diabetes. Approximately 50 percent of people diagnosed with diabetes are located in these three countries, according to the International Diabetes Federation (2013): China (98.4 million), India (65.1 million) and the USA (24.4 million).[2] India, a densely populated country, and equivalent to 17.7% of the total world population, is badly affected by the global epidemic of diabetes. Diabetes mellitus, is a disease that can be managed but lasts a lifetime.[3] As compared to Type 1 diabetes mellitus (T1DM), Type 2 diabetes mellitus (T2DM) is more predominant. Treatment of T2DM begins with oral antidiabetic drug monotherapy and combination therapy with insulin or glucagon-like peptide-1 (GLP-1) receptor agonists.[4] These agents increase the amount of insulin secreted by the pancreas, which enhances the sensitivity of the target organs to insulin, and the rate of glucose absorption from the gastrointestinal tract decreases. The main classes include agents that stimulate insulin secretion (sulphonylureas and rapid-acting secretagogues), improves insulin action (thiazolidinediones),reduces hepatic glucose production (biguanides) or delay digestion and absorption of intestinal carbohydrate (alphaglucosidase inhibitors).[5] However, due to their unpleasant side effects such as lactic acidosis, peripheral edema and abdominal pain, their clinical use is limited.[6] The Indian system of medicine has been using herbs as medicines for decades. Today, most of the Indian population depend on the use of the herbal medicines for their primary health needs.[7] Plant extracts or various folk plant preparations are recommended by traditional practitioners and often used by consumers for the treatment of diabetes without prescriptions.[8] Medicinal plants have many beneficial properties, including the prevention and restoration of ß-cell integrity and function, the management of insulin release, the enhancement of glucose absorption and usage and the regulation of the metabolism of carbohydrates through different

pathways.[9] The market is currently booming with various herbal formulations to treat diabetes, which consists of various herbs as its active constituents. Historically, herb-drug combinations have been used for curing several diseases.[10] However, frequent use of herbal medicines can affect the pharmacokinetics and pharmacodynamics properties of drugs and thus can cause Herb-Drug interactions (HDI). HDI may lead to synergistic, antagonistic and additive effects.[11] Pharmacokinetic interactions influence the absorption, distribution, metabolism or excretion of the drug and pharmacodynamic interactions can alter the pharmacologic efficacy of the drug. Motherwort, is used as traditional medicine because of its purported sedative and antispasmodic properties in European and Asian countries. When administered intravenously, motherwort reduces platelet aggregation and fibrinogen levels. It potentiates antithrombotic and antiplatelet effects and increases the risk of bleeding. Studies demonstrate that co-administration with benzodiazepines leads to synergistic sedative effect and may result in coma which is life threatening .[12] Majority of the HDIs are mediated through the cytochrome pathway. The cytochrome P450 (CYP) consists of the superfamily of hemeproteins and mainly the enzymes from CYP1, CYP2 and CYP3 families are known to catalyze the biotransformation of most of the clinically used drugs.[13] Many herbal medicines are known to act as inhibitors or inducers of the drug metabolizing enzymes. Thereby, the concomitant administration of these herbal medicines with drugs may lead to significant HDI.[14] However, the intricacy of the problem arises as many physicians are unaware of the possibility of occurrences of HDI. Also many of the patients consume herbal products without informing their physicians thereby raising the possibility of occurrence of HDI. Today, even though millions of people are using herbal supplements with the basic assumption that 'natural products' are 'safe' for consumption, there is very little information available on their safety. Hence, there exists an urgent need to educate and increase the level of awareness of occurrence of HDI among the patients. Also it was thought appropriate to collect information regarding the most commonly prescribed/consumed drugs and ayurvedic/herbal medicines used to treat diabetes mellitus. Accordingly, it was planned to assess the above parameters through a systematic survey.

MATERIAL AND METHODS
The study was conducted in rural and urban area of Pimpri Chinchwad in Pune, Maharashtra, India. This area is located about 20 km from Pimpri Chinchwad. The rural area comprises a group of 4 villages around the holy pilgrimage place of Alandi on the banks of the river Indrayani, while the urban area comprises the part of Pimpri Chinchwad Muncipal Corporation, India. The study was carried out in 1000 diabetic patients in duration of 6 months using a systematically designed questionnaire based health survey sheet (Table-01). The data was collected by an interview in person (95%) and by telephonic interview (5%). On visiting the house, members of the house, regardless of the gender were invited to participate in the study and were asked to fill the survey sheet. All those who willingly participated were included in this study. The record of the patients who declined to participate was excluded from the study. The outcome was based on the questions answered by the respondents. The questionnaire was designed in such a way so as to access the prevalence of diabetes mellitus in people of different age, sex, weight, type of diabetes, family history of the disease, whether associated with high BP, high cholesterol, and heart disease conditions, when diagnosed with diabetes etc. The questions included in the questionnaire also assessed the level of awareness of the respondents, like how frequently blood glucose levels are measured, whether they exercise, which allopathic medicines are consumed to control blood glucose level, cholesterol and blood pressure, dose of medicines, which herbal medicines are used, whether they are prescribed by doctors, and the effects observed on the blood glucose pattern. Also, questions 16 to 19 were framed to understand the level of awareness of the diabetes type 2 patients and the possibility of HDI.
The present study was approved by the Institutional Advisory Committee, Dr. D. Y. Patil Institute of Pharmaceutical sciences and Resaerch, Pimpri, Pune, Maharashtra, India.

RESULTS AND DISCUSSION
This study finding highlights the fact that the prevalence of DM in urban areas (10.5%) is increasing at an alarmingly rate as compared to rural population (6.5%). Patients in the urban population surveyed recorded higher weight with increased systolic blood pressure and cholesterol levels. However, the % of rural population with these disease conditions is also accelerating at an alarming rate, which probably represents the influence of unhealthy lifestyle practices that is slowing creeping into the rural areas. The analysis of the survey revealed that T2DM is more predominant (84.60%) among the respondents than T1DM (15.40%).This may be due to obesity, regional adiposity, higher percentage body fat which contributes to increasing the risk of DM. The variables independently associated with diabetes in adults include age, weight and family history of diabetes. Indians tend to have more body fat and are at a higher

risk of diabetes.[15] Another important finding of the present study was that the male population (60.15 %) showed higher prevalence of diabetes when compared to females (39.85%).The respondents in the weight category of 60-70 kg were found to show higher prevalence of diabetes than other weight groups. According to this study, most of the respondents were in the age group of 35-50 years. About 38% of respondents monitored their blood glucose level monthly, 9% bimonthly, 11% measured tri-quarter monthly, and 7% in a period of six months by using glucometer or in a pathology lab. It was observed that 24% respondents did not measure their blood glucose level regularly. 84.29 % of respondents reported no previous history of diabetes and only 15.71 % of the patients surveyed reported to have some genetic prevalence. The risk factors associated with diabetes were found to be high blood pressure (48.49%) and high cholesterol (20.78 %) in diabetic patients. People with diabetes are more likely to suffer from heart disease/ stroke, which is further complicated due to existing underlying medical complications like high blood pressure, high cholesterol, or both. About 57.21 % of the patients exercised regularly, which included walking, yoga (either early morning or evening), which helped them to control their blood glucose levels. Among the patients surveyed, 5.2 % of patient population was currently not undertaking any specific treatment or medical help for their diabetic condition. Majority of the respondents (67.80 %) were only consuming prescribed allopathic medications like metformin, glimepiride or glipizide as the basic mode of treatment. Study revealed that 15.40% the patients were consuming both oral hypoglycemic agents along with herbal preparations to control their blood glucose levels on the advice of their medical practitioners. 43.26 % respondents in the present study were of the opinion that herbal medicines demonstrated better efficacy, with minimal side effects and were more cost effective than the conventional medicines available for the treatment of diabetes. The consumption of Ayurvedic/herbal medicines, as observed, was higher (80.30%) among the female population as compared to males. The major herbs that were being consumed included juice of *Eugenia jambolana*, *Aloe vera, Momrdica chanrantia, Azadirachita indica, Curcuma longa.* The use of combination therapy was higher in the age group of 40 years and above. Many respondents also reported that Panchkarma therapy helped them to control their blood sugar levels. About 92.4% of respondents consuming herbal medicines along with prescribed medications were unaware of the possibility of occurrence of herb-drug interactions and its subsequent clinical consequences. Also only 15.78 % of the patients surveyed reported that their healthcare professionals enquired with their regarding the concomitant consumption of herbal products and counseled and cautioned the patients on the chances of development of HDl.

Table No-1 Survey questionnaire to study use of medications in type 2 diabetes mellitus and awareness of HDI

Name of the patient	
Address:	
Mobile No	
Date of birth	
Sex	□Female □Male
Weight	
Please indicate below which chronic condition (s) you have:	□Diabetes type 2 □Diabetes type 1
Others disease conditions	□High cholesterol□ High blood pressure □Heart disease □Others
Family history of diabetes, if any specify	
When diagnosed with diabetes	
How frequently do you record your blood glucose levels?	
Do you have a machine to measure blood sugar (glucose) level?	□Yes □ No
Do you exercise regularly?	□Yes □ No
Do you take allopathic medicines for diabetes? Please specify the name(s) and dose of the medicines you take:	□Yes □ No
Has the treatment provided effective control on blood glucose levels?	□Yes □ No
Have you been on insulin injections?	□Yes □ No
Do you take pills for high blood pressure?	□Yes □ No
Do you take pills for cholesterol?	□Yes □ No
Are you taking any ayurvedic/herbal formulation for treatment of diabetes? Please specify the name(s) and dose of ayurvedic formulation you take:	□Yes □ No
Is the ayurvedic/herbal formulation prescribed by doctor?	□Yes □ No
Have you observed any change in your blood sugar pattern?	□Yes □ No
Have you benefitted with ayurvedic /herbal co-therapy?	□Yes □ No
Is your physician aware that you also consume ayurvedic/herbal preparation?	□Yes □ No
Has your physician enquired with you regarding co-therapy?	□Yes □ No
Are you aware of possibility of Herb-drug interaction?	□Yes □ No
Whether physician advised you on the possibility of occurrence of HDI?	□Yes □ No
Are you continuing with the allopathic medicines also?	□Yes □ No

Table No-2 Response (respondents, %) to the survey questionnaire

	Questions	Response (Respondents, %)
1.	Age in years	(0-20: 7.4%), (20-40:14.80%), (40-60:54.3%), (60-80: 23.5%)
2.	Gender	Male (60.15%), Female (39.85%)
3.	Weight	Male (40-50 kg12.26 %), (50-60kg 15.42 %), (60-70 kg 60.1%), (70-80 kg 12.22%) Female (40-50 kg 6.37 %), (50-60kg 11.43 %), (60-70 kg 69.28%), (70-80 kg 12.92%)
4.	Type of Diabetes	T2DM (84.60%), T1DM (15.40%)
5.	Whether Family history of disease?	No (84.29 %), Yes (15.71 %)
6.	Other Diseases	High cholesterol (20.78%) High blood pressure (48.49%) Heart disease (29.73%) Lung disease (1%)
7.	When diagnosed with diabetes	Age in years (0-20:4.9 %), (20-40 12.8%), (40-60 65.42%), (60-80 16.88%)
8.	How frequently do you record your blood glucose levels	Monthly (38%), Bimonthly (9%), Tri-Quarterly (11%), Six monthly (6%), Irregular (24%)
9.	Do you have a machine to measure your blood sugar (glucose) level?	Yes (30.86%) No (69.14%)
10.	Do you exercise regularly?	Yes (57.21%) No (42.79%)
11.	Do you take allopathic medicines for diabetes?	Yes (67.80%) No (32.20%)
12.	Has the treatment provided effective control on blood glucose levels?	Yes (62.78%) No (37.22%)
13.	Have you been on insulin injections?	Yes (14.9%) No (85.1%)
14.	Do you take pills for high blood pressure?	Yes (49.37%) No (0 %)
15.	Do you take pills for cholesterol?	Yes (18.68 %) No (2.36 %)
16.	Are you taking any ayurvedic/herbal formulation for treatment of diabetes?	Yes (43 %) No (57 %) Female 80.30% male 19.70%
17.	Is the ayurvedic/herbal formulation prescribed by doctor?	Yes (15.40 %) No (84.6 %)
18.	Are you continuing with the allophatic medicines also?	Yes (70.1%) No (29.9%)
19.	Have you observed any change in your blood sugar pattern?	Yes (56.80 %) No (43.2 %)
20.	Have you benefitted with ayurvedic /herbal co-therapy?	Yes (43.77 %) No (56.23 %)
21.	Is your physician aware that you also consume Ayurvedic/Herbal preparation?	Yes (9.89 %) No (90.11 %)
22.	Has your physician enquired with you regarding co therapy?	Yes (15.78 %) No (84.22 %)
23.	Are you aware of possibility of Herb-drug interaction?	Yes (7.6 %), No (92.4%)
24.	Whether physician advised you on the possibility of occurrence of HDI?	Yes (4.5 %) No (95.5 %)

■ No of respondents on Allopathic treatment

■ No of respondents on combination therapy(Allopathic and Ayurvrdic /herbal medicines)

■ No of respondents who were on no treatment
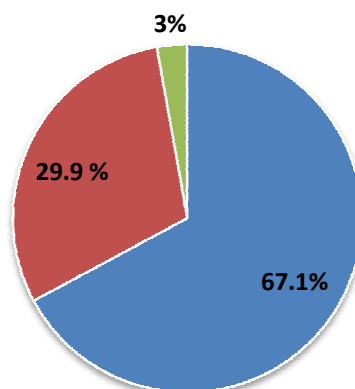
Fig 1. Statistics of use of Traditional and Allopathic Medicines

CONCLUSION

A systematic questionnaire based survey was carried out in the PCMC area (Pune District) of Maharashtra state in India for the assessment of treatment strategies adopted and awareness of Herb-Drug interactions in the treatment of diabetes mellitus. The analysis of data from respondents emphasized on the need for individuals to adopt a healthy food pattern, lifestyle with regular exercise to avoid such medical conditions. Also, it was observed that the majority of respondents were undertaking combination therapy of allopathic drugs with herbal/ayurvedic medicines, of which an alarming number (90.11 %) had not informed their physicians regarding the same. Also, it was noted that 95.5% of the physicians did not participate in the process of educating their patients on the need to report such practices. As literature reports that herb drug interactions can cause serious complications, the survey put forth the fact that there exists an earnest need to educate both the physicians and the patients on the possibility of occurrence of such HDI, which may arise on co-therapy of allopathic drugs and herbal medications. Hence, proper reporting of cases, careful vigilance, evidence based appraisal and constantly updated reviews of herb-drug interactions is essential to guide practitioners involved in patient care. Patient counselors and physicians should be familiar with the potential effects of commonly used medications to prevent, recognize and treat potential adverse effects associated with their use. The study findings also highlight the need for patient counselors and physicians to update their practice through additional training. Integration of their knowledge and expertise to study, identify, report and advice patients on such herb-drug interactions is vital to improve the therapeutic outcomes and safety of patients on anti-diabetic therapy.

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