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## Table of Content

Manuscript Title	Page No.
SEADFCON 2017 “Quality diabetes care beyond socio cultural barriers” Maskey R., Gupta PP., Kattel V.	1-2
Insulin Prescription Pattern among Type 2 DM patients visiting Outpatient Department at a Tertiary Hospital in Kathmandu, Nepal Hari Kumar Shrestha, R Tamrakar, Ashish Shrestha, SR Amatya	3-7
Cognitive Effect of Standardized group education programme in Diabetic population Ravi Kant, Meenakshi Khapre, Amninder Singh	8-11
Awareness of Symptoms and Early Management of Hypoglycemia among Patients with Diabetes Mellitus Suresh K. Sharma, Ravi Kant	12-17
Response to Cabergoline treatment in Invasive Prolactinoma with hemorrhage- A case report Vivek Pant, Suman Baral, Binod Aryal, Arjun Tumbapo	18-20
About the Journal	21-24



## SEADFCON 2017 theme “Quality diabetes care beyond socio cultural barriers”

Maskey R., Gupta PP., Kattel V.

Diabetes is emerging as a major global problem worldwide and is reaching epidemic proportions with global prevalence of 8.3%, affecting 387 million adults and costing 612 billion dollars in health care spending in 2014.<sup>1</sup>The IDF estimates that the prevalence of DMT2 in Nepal was 4.5% in 2012 and the predicted number of undiagnosed cases in adults was 294 per 1000 population. Relative to neighbouring countries such as Pakistan, Sri Lanka, and Bangladesh, Nepal has a higher prevalence of DMT2 and impaired glucose tolerance.<sup>2</sup>

Diabetes is a particular problem in the South Asian community, as people from this ethnic origin are four times more likely to develop the condition than other groups.<sup>3</sup>South Asian people with type 2 diabetes also have a greater risk of developing cardiovascular disease and renal problems, and a higher diabetes-related mortality rate is seen among this group than in the general population.<sup>4</sup>

Diabetes especially type 2 diabetes is an emerging major health care problem in Nepal, with rising prevalence and its complications especially in urban populations. Several challenges in diabetes management were identified, including high cost of treatment, limited health care facilities, and lack of disease awareness among patients.

The economic burden of diabetes is enormous. Diabetes is costly because of its chronic nature, the severity of its complications, and the modalities required to control them.<sup>5</sup>Consequently, people have frequent and intensive encounters with the health system such as higher use of hospital inpatient care, outpatient visits, emergency visits, and prescription drugs. Moreover, the out-of-pocket expenses associated with diabetes remain a barrier to the prevention of diabetes-related complications in Nepal.<sup>6</sup>

Culture is a shared and dynamic phenomenon displayed by the behaviours and attitudes of a social group, which remains difficult to interpret, but requires a good understanding by health workers.<sup>7</sup>It encompasses beliefs, language, social norms and values, including practices which can create a sense of social support and belonging for individuals who share the same core beliefs. These can both facilitate and impede health coping styles, access to and utilisation of healthcare services, and implementation of professional advice.<sup>8</sup>

Prevention or delay of diabetes in this population would improve quality of life and reduce health care costs. Identifying cultural definitions of health and diabetes is critically important to developing effective diabetes prevention programs.

We conclude that a comprehensive national effort is needed to stem the tide of the growing burden of diabetes mellitus type 2 and its complications in Nepal. The government should develop a comprehensive plan to tackle diabetes and other non-communicable diseases supported by appropriate health infrastructure and funding.

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## Original Research



# Insulin Prescription Pattern among Type 2 DM patients visiting Outpatient Department at a Tertiary Hospital in Kathmandu, Nepal

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## Abstract

**Background:** Management of Type 2 Diabetes Mellitus includes non-pharmacological and pharmacological interventions of which insulin remains one of the most effective methods for achieving glycemic control, either alone or in combination with oral anti-diabetic medications. Effective usage of insulin in the management of glycaemia remains a challenge in developing countries like Nepal. To best of our knowledge, there is not any study regarding insulin prescription pattern on Type 2 Diabetes Mellitus patients using insulin from Nepal, so we studied the prescription pattern of insulin on insulin using Type 2 Diabetes Mellitus patients.

**Methods:** Patients aged 30 years or above who present in Dhulikhel Hospital outpatient clinic during the period from January 2015 to June 2015 with diagnosis of Type 2 Diabetes Mellitus diagnosed at least for 6 months and were taking injection insulin at least since last 3 months were enrolled in this cross sectional, observational study.

**Results:** Forty-five study participants had a mean age of  $56.6 \pm 10.95$  year, body mass index of  $23.97 \pm 4.72$  kg/m<sup>2</sup>, Diabetic duration of  $10.33 \pm 6.41$  years and HbA1c of  $8.53 \pm 1.53\%$ . Fifty-three percent were female and almost all study participants (96%) were taking Oral Antidiabetic Drugs along with Insulin. Sixty-three percent of participants were using Premix insulin whereas 33% were using basal insulin alone. Mean Insulin dose was  $28.96 \pm 11.75$  units per day. Among them, 80% were "self" injecting insulin and 53% were using Glucometer.

**Conclusion:** Our data showed that premixed insulin being most commonly used insulin. All patients used Insulin Pen as delivery device and larger proportions of them were self injecting insulin. All patients felt mild hypoglycemia which can be improved by increased utilization of glucometer.

**Keywords:** hypoglycemia; insulin; T2DM

## INTRODUCTION

Diabetes Mellitus (DM) is a metabolic disorder characterized by prolonged hyperglycemia due to inadequate insulin secretion or defective insulin action or both. It is estimated that, more than 70% of people with diabetes will reside in developing countries by 2030.<sup>1</sup> Achieving good glycemic control has important role in reducing the burden of disease attributable to diabetes mellitus.<sup>2</sup>

Management of DM includes non-pharmacological and pharmacological

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interventions of which insulin remains one of the most effective methods for achieving glycemic control, either alone or in combination with oral anti-diabetic medications.<sup>3,4,5</sup> According to recent estimates, nearly 40% patients with T2DM in India and Gulf countries are using insulin alone or in combination with OADs at any given point of time.<sup>6, 7</sup> There is one study on prescription pattern in DM patients attending outpatient clinic of a tertiary hospital from Nepal documenting 15% were using insulin.<sup>8</sup> Effective usage of insulin in the management of glycaemia remains a challenge in developing countries like Nepal. Proper insulin administration can also prevent



many of the adverse outcomes associated with it especially hypoglycemia, lipodystrophy, rash.<sup>9</sup>

To best of our knowledge, there are not any study regarding insulin prescription pattern and assessing hypoglycemia on DM patients using insulin. Thus this study was performed to assess the prescription pattern and hypoglycemic awareness on insulin using type 2 diabetic patients.

## METHODS

This was a cross sectional study done in patients aged 30 years or above who present in Dhulikel Hospital outpatient clinic with diagnosis of Type 2 Diabetes Mellitus diagnosed at least for 6 months and were taking injection insulin at least since last 3 months from January 2015 to June 2015. Patients with any major illness, surgery, or diabetic ketoacidosis in last 6 months, use of glucocorticoids, post-transplant diabetes, and gestational diabetes were excluded. This study was approved by Institutional Research Committee of Kathmandu University. Sampling methods, technique and sample size calculation

A questionnaire form was made and patients were asked their demographic information including name, sex, age, marital status, educational level, smoking and alcohol history. Physical examination was done at the time of enrollment including measurement of height, weight, and blood pressure. For blood pressure measurement, patients were asked to do rest at least for 5 minutes and taken two blood pressure measurements consecutively at 5 minutes interval and taken mean value as patients BP. Information about diabetic history, diabetic complications and medical treatments were assessed. Lastly, recent laboratory results of fasting plasma glucose (FPG), HbA1c, LDL level were recorded. Lab results of previous 30 days (fasting blood lipid and HbA1c results within 3 months) were accepted for the study.

Chi-square test was used to compare qualitative variables, if this was inappropriate then nonparametric test was used. For quantitative variables, Tests of normality was done and found that all such variables were not distributed normally. Nonparametric test (2 independent sample test) was used for such variables. P <0.05 was considered statistically significant. All data were analyzed using SPSS 20.

## RESULTS

In this cross-sectional study, 150 diabetic patients were enrolled. The mean age of the patient was 56.6 years (SD: 10.95). Fifty-three percent of the patients were female. The mean Diabetes duration was found to be 10.33 years (SD: 6.41). The mean HbA1c was 8.53% (SD: 1.53). Variables are tabulated on Table 1.

Table 1. Clinical parameters of study participants

Variables	n; Mean $\pm$ SD
Age (years)	56.6 $\pm$ 10.95
DM Duration (years)	10.33 6.41
BMI (kg/m <sup>2</sup> )	23.97 4.72
FBS (mg/dl)	137.88 $\pm$ 49.56
HbA1C (%)	8.53 $\pm$ 1.53
Variables	n (%)
Gender, n (%) Male	21 (46.66)
Female	24 (53.33)
Education, n (%)	
Below SLC	21 (46.6)
Intermediate	16 (35.6)
Bachelor and above	8 (17.8)
Known case of Dyslipidemia	21 (46.7%)
Known case of Hypertensive	15 (33.33%)

The proportion of patients according to age group is shown in Figure 1, whereas Figure 2 illustrate according to diabetic duration; with almost half were having diabetic duration more than 10 years.

## % of patients

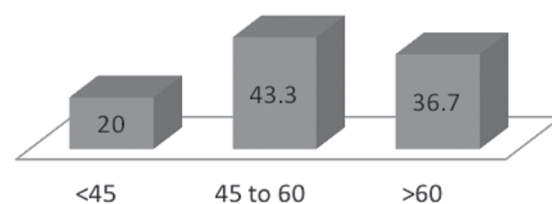


Figure 1: Bar diagram showing % of patients according to age distribution

## % of Patients

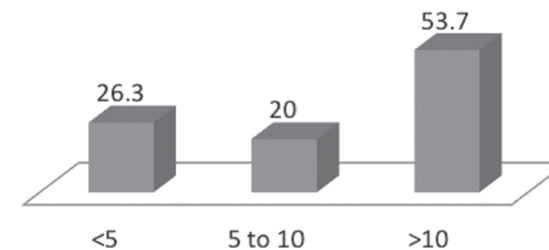


Figure 2: Bar diagram showing percentage of patients according to Diabetic Duration distribution

## % of Insulin

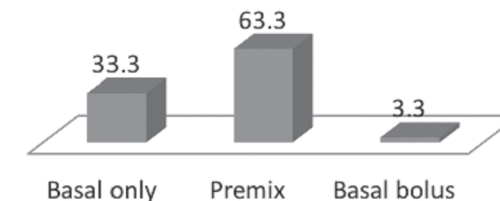


Figure 3: Bar diagram showing percentage of insulin prescription regimen

In this study, most common form of insulin prescription was Premix insulin as seen in Figure 3. Only one patient was prescribed basal bolus regimen. One third of patients was prescribed Analogue insulin whereas Regular insulin being the most common type of insulin as described in Figure 4. Mix subgroup shown in Figure 4 meaning premix insulin formed with combination of short acting analogue insulin and NPH insulin whereas Regular subgroup meaning premix insulin formed with combination of short acting regular insulin and NPH.

## % of Patients

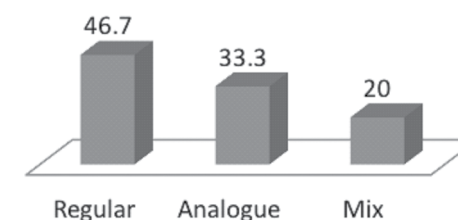


Figure 4: Bar diagram showing percentage of insulin prescription based on its type

Table 2. Treatment characteristics of insulin treated T2DM patients.

Variables	n (%)
Medication regimen	
Insulin alone	9 (20)
Insulin and OAD	36 (80)
Insulin Pen as insulin delivery device	
Yes	45 (100)
No	0 (0)
Self Insulin Injection	
Yes	36 (80)
No	9 (20)
Using Glucometer	
Yes	24 (53.3)
No	21 (46.7)
Self-Reported Hypoglycemia symptoms,	
Yes	45 (100)
No	0 (0)
Variables	n; Median SD
Insulin (Unit/day)	28.96 11.75
Insulin Duration (months)	12.10 10.41

## DISCUSSION

The mean age and diabetes duration were similar to the baseline data from other studies,<sup>10-12</sup> one being a multinational prospective observational study (MOSAIC) addressing similar issues amongst T2DM patients on insulin with or without OADs.<sup>11</sup> In our study, 53% of participants are female, similar with Chinese cohort of MOSAIC but higher comparing to Indian cohort, which could be due to referral bias. Education status of our patients is also comparable to other studies,<sup>10, 11</sup> more than fifty percent of them had graduated High School, which is 57% in Indian cohort of MOSAIC. In our study, mean  $\pm$  SD HbA1c was 8.53  $\pm$ 1.53 %, comparable with recently conducted DiabCare Asia trials in India and Gulf countries showing 8.9  $\pm$  2.1 % and 8.3  $\pm$  2.0 % respectively.<sup>13, 14</sup>

Eighty percent of our study participants were using insulin along with OADs which is similar with Indian and Saudi Arabian cohort of MOSAIC.<sup>11</sup> Other studies<sup>10, 15</sup> showing higher rate of sole insulin usages. Higher usages of OADS along with insulin in our study may be acknowledging the pathophysiology of T2DM as proposed by Ralph A DeFronzo.<sup>16</sup>

Nearly 2/3rd of our patient were prescribed premix insulin (human or analog), aligning with evidences from previous real world data, epidemiological surveys, and consensus statements of key opinion leaders.<sup>10, 13, 17, 18</sup>

Our patients were prescribed slightly higher analog insulin similar with Indian study documenting 10 years audit of insulin injection practices.<sup>10</sup> In our study, 46.7% used only human insulin, 33.30% used only analog insulin and 20% used both regular and analogue insulin. The comparative figures for human versus analog were 71% versus 32% in the DiabCare India study,<sup>13</sup> 68.3% versus 31.7% in the Japanese GP study<sup>19</sup> and 26% versus 85% in DiabCare Gulf study.<sup>14</sup> Such variations of choice may have been influenced by many factors, among them socioeconomic conditions, affordability, availability being main player.

TDD of insulin (U/day) was 28.96 ± 11.75 in our study, which was similar to Indian audit of Insulin Injection Practices<sup>10</sup> and DiabCare India survey<sup>13</sup> which reported 33.36 ± 18.34 and 32.1 ± 17.0 respectively. While the DiabCare Gulf study<sup>14</sup> used higher mean daily dose (U/day) of 57.5 ± 30.4, their Japanese GP study<sup>19</sup> reported relatively lower dose of 25.8 ± 22.9 U/day. Such finding may indicate racial variations in daily requirement of insulin in addition to a different pattern of practice amongst practitioners of a particular country or region.

In our study, all patients used insulin pen device, in concordance with Chinese (100%) and Germany (95%) cohort of MOSAIC study.<sup>11</sup> In Indian audit of Insulin Injection Practices<sup>10</sup> pen device was used by 66.08% of the patients, whereas 31.76% patients used insulin syringes, and 2.15% were using both Insulin pen as well as syringes. Similarly, In DiabCare India study 65.6% used pens, 32.0% used syringes.<sup>13</sup> Data from a recent large worldwide survey indicated that insulin pen alone was used by 85.6% of patients, while 9.6% used a syringe alone, 2.8% used both, and 1.4% used a pen and another device (usually an insulin pump).<sup>20</sup> Thus, it seems economic condition is an important, but not the sole factor responsible for, physicians or patients choice and familiarity in using modern devices during insulin therapy also may have important role. In this study, 80%

were self injecting insulin, similar with Nigerian Study.<sup>12</sup>

The American Diabetic Association (ADA) has recommended SMBG using glucometer in all diabetic patients on insulin.<sup>13</sup> However, almost half of our study patients did not have access to glucometer despite being on insulin therapy. Other studies from developing countries like India<sup>10</sup> reported that one third of patients were not using glucometer while Nigerian<sup>12</sup> and Pakistani study<sup>21</sup> reported 56% and 59% of Type 2 Diabetic patients were utilizing glucometer respectively.

In this study, all patients reported mild form of hypoglycemia, similar with an Indian study conducted among 366 Type 2 Diabetic Patients where 96% reported hypoglycemic symptoms.<sup>22</sup> A met analysis involving 532,542 People with Type 2 Diabetes on Oral Therapies and Insulin reported that prevalence of mild/ moderate hypoglycemia was 50%<sup>23</sup> whereas Nigerian study [12] reported it among 65% patients. In contradiction, only 7.6% of participants reported hypoglycemia in Indian audit of Insulin Injection Practices.<sup>10</sup>

### CONCLUSIONS

Our data showed that premixed insulin being most commonly used insulin. All patients used Insulin Pen as delivery device and larger proportions of them were self injecting insulin. All patients felt mild hypoglycemia which can be improved by increased utilization of glucometer.

The one limitation of this study is that the sample size was small and it was study done in single hospital setting.

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### CONFLICT OF INTEREST

The Author disclosed that there is no conflict of interest in publishing this research paper.

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## Cognitive Effect of Standardized group education programme in Diabetic population

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### Abstract

**Background:** The prevalence of diabetes in India has reached alarming levels with 8.7% of population affected as of 2015, which is expected to double in the future. The reasons for the rapid increase in prevalence of diabetes include genetic predilection of Indian population, economic boom, sedentary lifestyle, inadequate follow up and lack of disease awareness. The aim of the study was to overcome the self care deficit which would help patients to be more compliant and better in managing their illness.

**Methods:** The study was conducted at weekly diabetes clinic at AIIMS, Rishikesh in which 200 patients participated. Two sessions, each of 60 minutes were conducted fortnightly. The patients were educated by trained personnel using specially designed module in patients' own language. Each group consisted of 10- 15 participants. Participants were tested at the beginning and after the educational programme using a 10 item questionnaire. Data was analysed using MS Excel 2010. Paired t test was used to find any significant difference between pre and post test score.

**Results:** A significant improvement in test scores after education session was noted. Average learning gain was 77.98 %  $\pm$  23.27 % after the group education. Sixty four percent participants demonstrated more than 75% learning gain.

**Conclusion:** A dedicated group session programme implemented in an environment conducive to learning with specially designed module has a significant impact on patients' knowledge (64% participants demonstrated more than 75% learning gain) about the cause and treatment of their disease. The study can be extended to see if it impacts behaviour by tracing changes in glycaemic control.

**Keywords:** cognitive; diabetes; education

### INTRODUCTION

Indian diabetes federation had mentioned 69.1 million cases of diabetes in India in 2015 with prevalence of 8.7 % that will be doubling in near future<sup>1</sup>. Indian healthcare professionals and patients in India face a number of challenges such as clinical inertia in achieving glycaemic control, inadequate follow-up and lack of disease awareness.<sup>2, 3</sup>

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Orem theory of self-care is framework for integration of self-care concept into patient education and adherence. Self-care is behaviour from life situation that person directs to themselves or their environment to regulate factors affecting their own development, health or wellbeing. It is a learnt and goal oriented behaviour<sup>4</sup>. Self-care deficit exists when self-care demand is not met for which patient education is the solution. The American Diabetes Association recommends assessment of self-management skills and knowledge of diabetes at least annually, and the provision or encouragement of continuing diabetes education<sup>5</sup>

This study is done to overcome the self care deficit which would help patients to be more compliant and better in managing their illness.

### METHODS

This study was conducted in weekly diabetes clinic of All India Institute of Medical Sciences, Rishikesh. Type 2 diabetes patients of Rishikesh, regardless of how long they had been living with diabetes, with low functional health literacy attending the diabetes OPD were included in the study. The Ethical approval was given by the Institutional Ethics Committee. Two hundred patients were recruited after obtaining their consent. Participants were pre- informed of their sessions either by phone or message. Two sessions were conducted fortnightly. Each group consisted of 10- 15 participants excluding the support i.e. family members. Each session was conducted for a period of 60 min followed by discussion, recall, comprehension and feedback thereby completing the communication loop<sup>8</sup>. Trained junior resident and health worker facilitated the sessions. Module was prepared by expert faculties in diabetes and tailored to the needs of the patients in Hindi language. Interactive sessions in the form of videos, Power Points and problem solving were held.

The topics included were as given by National Standards for DSME<sup>5</sup>.

- Describing the diabetes disease process and treatment options
- Incorporating nutritional management into lifestyle
- Incorporating physical activity into lifestyle
- Using medication(s) safely and for maximum therapeutic effectiveness
- Monitoring blood glucose and other parameters and interpreting and using the results for self-management decision making
- Preventing and delaying complications
- Developing personal strategies to address psychosocial issues and concerns

They were given some task on basis of topic taught to transfer the knowledge in everyday life which was reviewed in next session. Defaulters were motivated to attend next sessions.

Disease knowledge test was used to evaluate basic knowledge about diabetes. Participants were tested at the beginning and after the educational program. A 10-item questionnaire was used to assess diabetes-related knowledge

and self-care practices, each answer scoring one point, up to a maximum of 10.

Data was analysed using MS Excel 2010. Paired t test was used to find any significant difference between pre and post test score. Average learning gain was computed by Pre – post / 10- pre X100.

### RESULTS

In this study there were 93 (46.5 %) female participants and 107 (53.5 %) males. Maximum females were between 40- 50 years (34.4 %). Maximum males were in age group of 60- 70 years (42.99%). Overall 36 % were in age group of 60- 70 years followed by 40 – 50 years (24.5 %) and 50- 60 years (21.5 %) (Table 1).

Table 1. Age and sex distribution of participants

Age	sex		Total
	F	M	
20-30	1 (0.01%)	3 (2.8%)	4 (2%)
30- 40	12 (12.9%)	15 (14.01%)	27(13.5%)
40- 50	32 (34.4%)	17 (15.89%)	49 (24.5%)
50- 60	19 (20.4%)	24 (22.4%)	43 (21.5%)
60- 70	26 (27.95%)	46 (42.99%)	72 (36%)
70- 80	3 (0.032%)	1 (0.93%)	4 (2%)
>80	0	1 (0.93%)	1(0.5%)
Total	93(100%)	107 (100%)	200 (100%)

8. Average learning gain was 77.98 %  $\pm$  23.27 % after the group education (Table 2).

Table 2. Changes in Pre-test and post-test score after Standardized group education

Score	Pre test score	Post test score
< 5	73 (36.5 %)	4(2 %)
5 -8	112 (56 %)	62(31 %)
> 8	15 (7.5 %)	134(67 %)
Total	200(100 %)	200 (100 %)
Mean	5.29	8.79
SD	2.111	1.448
Paired t test	31.27 P= 0.0001	

There was no sex wise difference in learning gain among participants (Table 3). Sixty four percent of participants demonstrated more than 75 % of learning gain. While geriatric participants demonstrated significantly lesser

learning gain compared to their middle aged and younger participants. (Table 4)  
Table 3. Sex-wise distribution of average learning gain

Average Learning gain	Sex		Total	X <sup>2</sup>
	Female	Male		
< 50 %	20 (21.5%)	12 (11.2%)	32 (16%)	3.971 p- 0.137 NS
50 – 75 %	18 (19.35%)	22 (20.5%)	40 (20%)	
>75 %	55 (59.13%)	73 (68.22%)	128 (64%)	
Total	93 (100%)	107 (100%)	200 (100%)	
Average learning gain	77.98 % ± 23.27 %			

Table 4. Age -wise distribution of average learning gain

Average Learning gain	Age		Total	X <sup>2</sup>
	<60 yrs	> 60 yrs		
< 50 %	20 (14.6%)	12 (19.04%)	32 (16%)	7.786 p-0.02
50 – 75 %	21 (15.3%)	19 (30.15%)	40 (20%)	
>75 %	96 (70.1%)	32 (50.8%)	128 (64%)	
Total	137 (100%)	63 (100%)	200 (100%)	

## DISCUSSION

Group education programme for diabetes was found to be effective in many studies<sup>9-11</sup>. Also the challenges faced by diabetes patients are akin to each other. Therefore, this standardized group educational programme was planned. Keeping in mind about feasibility of patient to return back for sessions, only two sessions totalling 2-hours in duration at interval of 15 days were planned.

Studies<sup>9-12</sup> have proven the effectiveness of patient education programme by improvement in their knowledge on the disease, glycaemic control and BMI. Changes in BMI, glycaemic control need around 6 months to exhibit, so only change in knowledge score is unveiled in this study, long term benefit study is going on. In this study we found significant improvement in knowledge score of patient after the group education sessions. Improvement in learning for all participants was outstanding.

No difference in average learning gain was found in sexes. Older Age was found to be a significant factor that affects the learning process. We therefore also invited one care giver in these sessions as support system helps in achieving better compliance and transfer of knowledge. Improvement in pre and post test score was more in those who scored less in pre-test and vice versa corresponding to results of other study<sup>12</sup>. Patients felt free to ask question and express opinion regarding their socio-cultural and psychological issues. Sharing each other's experiences on coping with the diabetes was appreciated by participants as it gave them a platform to discuss their psycho-social problems. Also, the programme helped them to have an open dialogue with health care providers.

With the growing burden of diabetes and out of pocket expenditure to individual, achieving the therapeutic goal and preventing the

complications is of utmost importance. Diabetes education plays an important role in management of diabetes. This group education programme was found to be feasible, effective and acceptable to patients. This group education programme can be implemented on routine basis for all diabetic patients and one refresher session of one hour per year.

## CONCLUSIONS

A dedicated group session programme implemented in an environment conducive to learning with specially designed module has a significant impact on patients' knowledge (64% participants demonstrated more than 75% learning gain) about the cause and treatment of their disease. The study can be extended to see if it impacts behaviour by tracing changes in glycaemic control.

## CONFLICT OF INTEREST

There are no conflicts of interest with any of the authors

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## Awareness of Symptoms and Early Management of Hypoglycemia among Patients with Diabetes Mellitus

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### Abstract

**Background:** Hypoglycemia mostly occurs in diabetic patients on medications. Lack of awareness on hypoglycemic symptoms among patients may delay its identification and treatment. The symptoms of hypoglycemic symptoms among patients may delay its identification and treatment. Neglecting the symptoms of hypoglycemia and delaying treatment could cause poorer outcomes or morbidity. The present study was aimed to assess the awareness of symptoms of hypoglycemia and knowledge in early management of hypoglycemia among patients with diabetes.

**Methods:** A Cross sectional study was done among 500 diabetes mellitus patients attending the outpatient department of AIIMS, Rishikesh, Uttarakhand in 2017. Patient with diabetes for over five years and who were on insulin treatment were included in the study. After obtaining an informed consent, knowledge on the symptoms and early treatment of hypoglycemia were collected. The data were analyzed by frequency and percentage.

**Results:** The study included 500 diabetic patients, of which 55.5% were females. The common symptoms of hypoglycemia known to the study subjects were dizziness (84.4%), weakness (74.1%), and drowsiness (68.1%). Overall, 322 (64.4%) diabetic patients had good knowledge on hypoglycemia (knowledge of at least three symptoms of hypoglycemia together with at least one precipitating factor and at least one remedial measure). Regarding management of hypoglycemia, 49% patients preferred taking glucose powder or sugar with water as an immediate measure. Higher age, illiteracy, low socioeconomic status was associated with poor knowledge whereas treatment with insulin along with oral hypoglycemic agents was associated with good knowledge on hypoglycemia.

**Conclusion:** Although the knowledge on the symptoms, remedial measures, and prevention of hypoglycemic episodes was good among the type 2 diabetic patients in the study, there were gap in knowledge on important aspects like precipitating factors, target levels etc., which need to be addressed by health care workers through regular educational programs.

**Keywords:** Diabetes mellitus, hypoglycemia, awareness, management, insulin.

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**Background :** The symptoms of hypoglycemia may be nonspecific with intensity decreasing with increasing age. Thus, it is very important that the subjects are able to recognize and identify the symptom onset at an early stage in order to manage the episode effectively and take steps to prevent the recurrence. Neglecting the symptoms of hypoglycemia and delaying treatment could cause poorer outcomes or morbidity.

Large trials (action to control cardiovascular risk in diabetes, Veterans affairs diabetes trial) have shown that there were was a higher mortality in the group that had hypoglycemia (intensively treated arm)., Hence, the American Diabetes Association (ADA) guidelines emphasize on individualizing targets and reducing risk of hypoglycemia in patients with long duration of diabetes and comorbidities. In a survey conducted by the American Association of Clinical Endocrinology emphasize that there was a knowledge gap which most be addressed.

In this background, the knowledge and awareness about the varied presentations of hypoglycemia and the possible early management strategies for the same would go a long way in patients with diabetes management. There is a need for shared responsibility in the prevention of hypoglycemia. We proposed to study the knowledge about hypoglycemia and its early management among diabetes patients attending AIIMS, Rishikesh.

**Methods :** This cross sectional study study was done among purposively selected 500 diabetes mellitus patients for over five years and who were on insulin treatment attending the Diabetic Clinic of All India Institute of Medical Sciences (AIIMS), Rishikesh, Uttarakhand. Study was conducted during June 2016 to July, 2017.

Patients with diabetes mellitus-I, DM-II patients receiving only oral hypoglycemic drugs, pregnant women with gestational diabetes mellitus, diabetes secondary to other systemic diseases were excluded from the study. This study was approved by Institute Ethical Committee and after obtaining an informed written consent, patients were subjected to a semi-structured interview to assess the

knowledge on the symptoms and early treatment of hypoglycemia along with base line data about the patient and disease existence.

The questions related to knowledge of the diabetic patients on the symptoms of hypoglycemia, the precipitating factors of such attacks, the immediate remedial measures which need to be adopted by them, the complications and how to prevent further episodes were also asked to them. For each of the above question, multiple responses were given, and the patients were asked to give a "yes or no" response. Multiple responses were also accepted. Patients were interviewed only once during the during the period of data collection, even if they came for follow-up visits regularly. The data were analyzed by frequency and percentage.

**Results :** The study included 500 diabetic patients, more than half of the patients (55.5%) of the study subjects were females. The mean age (standard deviation [SD]) of the study participants was 59.6 (±9.7) years and the age ranged from 29 to 85 years. Majority of the patients (81%) were more than 50 years of age and were belonging to middle socioeconomic class (80%). The mean (SD) duration of diabetes was 10.9 (±5.9) years with a duration ranging from 6 to 40 years (Table 1).

Table1: Background characteristics of patients with Diabetes Mellitus N=500

Back Ground Characteristics	f (%)
<b>Age in Years</b>	
1. Up to 50	95 (19)
2. 51-60	200 (40)
3. > 60	205 (41)
<b>Sex</b>	
1. Male	223 (44.5)
2. Female	277 (55.5)
<b>Education</b>	
1. Illiterate	280 (56)
2. Literate	220 (44)
<b>Monthly Income</b>	
1. Rs. ≤ 5000/-	66 (13)
2. Rs. 5001 – 10,000/-	34 (7)
3. Rs. 10,001 – 15,000/-	251 (50)
4. Rs. 15,001 – 20,000/-	115 (23)
5. Rs. ≥ 20,001	34 (7)
<b>Duration of Diabetes Mellitus</b>	
1. < 5 years	76 (15)
2. 5 – 10 years	230(46)
3. >10 years	194 (39)

The common symptoms of hypoglycemia known to the study subjects were dizziness (84.4%), weakness (74.1%), and drowsiness (68.1%). Headache (19.7%) and seizures (2.7%) as symptoms were known to less number of patients only (Table 2). Overall, 322 (64.4%) diabetic patients had good knowledge on hypoglycemia (knowledge of at least three symptoms of hypoglycemia together with at least one precipitating factor and at least one remedial measure) and 56 (11.2%) patients were not known even one symptom of hypoglycemia.

Table 2: Knowledge of symptoms of hypoglycemia among Diabetic patients N=500

Knowledge of Symptoms of Hypoglycemia	
Symptoms *	f (%)
Dizziness	422 (84.4)
Drowsiness	341 (68.1)
Excessive hunger	355 (71)
Sweating	25 (45)
Seizures	14 (2.7)
Head ache	99 (19.7)
Weakness	365 (73)
Loss of conscious ness	195 (39)
confusion	175 (35)
shaking	165 (33)
*multiple response were allowed	

More than two-thirds (68.6%) of the patients knew that hypoglycemia may be precipitated by missing or delaying of meals. Exertion as a precipitating factor was known to 35.2% of patients (Table 3). At least one precipitating factor was known to 389 (77.8%) patients and remedial measure, anyone, to be taken during an episode was known to 451 (90.2%) of patients. Half of the patients (49.7%) did not know even one complication of hypoglycemia.

Table3: Knowledge of precipitating factors of hypoglycemia and its remedial and preventive measures among Diabetic patients\*  
N=500

Factors & Measures	f (%)
<b>Precipitating Factors</b>	
1. Missing or delayed food	343 (68.6)
2. Exertion	176 (35.2)
3. Wrong dosage	140 (28)
4. Alcohol intake	40 (8)
<b>Complication of Hypoglycemia</b>	
1. Paralytic attack	185 (37)
2. Heart attack	180 (36)
3. Coma	175 (35)
4. Death	165 (33)
5. Fits	75 (15)
<b>Remedial measures during Hypoglycemia</b>	
1. Glucose powder or sugar	245 (49)
2. Go to casualty or emergency department	325 (65)
3. Eat food	195 (39)
4. Drink sugar syrup	305 (61)
<b>Preventive measures</b>	
1. Take timely meal	460 (92)
2. Take medication as advised	430 (86)
3. Report to doctor	240 (48)
4. Adjust the medications	-
5. Self-monitoring blood sugar	370 (74)
*multiple responses allowed	

Regarding management of hypoglycemia, 49% patients preferred taking glucose powder or sugar with water as an immediate measure. Majority of patients (65%) felt going to the casualty or emergency department was the right option for hypoglycemia. Eating food which is either missed or delayed as a measure to be taken during an episode of hypoglycemia was known to <40% of the study population.

Upon questioning their knowledge on prevention of further attacks, most of the patients (92%) mentioned "taking timely meals" as a measure and 87%, to take medications as per prescriptions of the doctor. Only a fifth of the patients were aware of "self-monitoring of blood glucose (SMBG) by glucometers" as a means to prevent further attacks as this will help them to identify hypoglycemia at an early stage, correlate with symptoms and take preventive measures (Table 3).

Thus, overall 331 (66.2%) diabetic patients had knowledge of at least three symptoms of hypoglycemia together with at least one precipitating factor and at least one remedial measure and therefore were considered to have good knowledge on hypoglycemia. Higher age, illiteracy, low socioeconomic status was associated with poor knowledge whereas treatment with insulin along with oral hypoglycemic agents was associated with

good knowledge on hypoglycemia. Sex and duration of disease were not associated with knowledge on hypoglycemia.

More than 50% of the patients attributed their knowledge of hypoglycemia to the doctor who treated them. A little lesser proportion (42.6%) attributed their knowledge to their friends and relatives. A quarter learnt about hypoglycemia from the fellow patients who get treatment from the OP clinic (Figure 1).

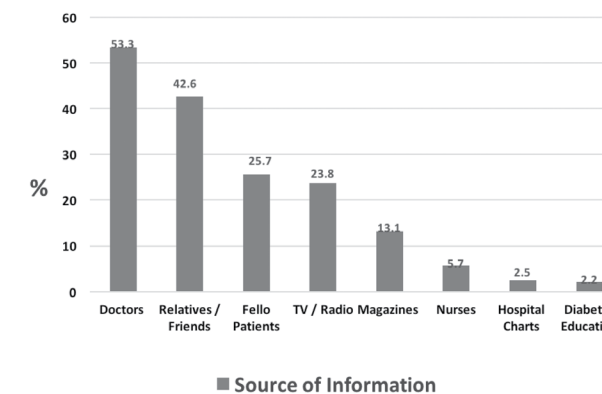


Figure 1:Source of knowledge on hypoglycemia among Diabetic Patients

## Discussion

The study included 500 diabetic patients, more than half of the patients (55.5%) of the study subjects were females. The mean age (SD) of the study participants was 59.6 ( $\pm 9.7$ ) years and the age ranged from 29 to 85 years. Majority of the patients (81%) were more than 50 years of age and were belonging to middle socioeconomic class (80%). The mean (SD) duration of diabetes was 10.9 (5.9) years with a duration ranging from 6 to 40 years. Higher age, illiteracy, and low socioeconomic status were associated with poor knowledge whereas treatment with insulin along with OHAs was associated with good knowledge on hypoglycemia. Sex and duration of disease were not associated with knowledge on hypoglycemia.

Diabetes is fast gaining the status of a potential epidemic in India with more than 62 million diabetics. According to Wild et al the prevalence of diabetes is predicted to double globally from 171 million in 2000 to 366 million in 2030 with a maximum increase in India. It is predicted that by 2030 diabetes mellitus may afflict up to 79.4 million individuals in India.

With respect to the knowledge on symptoms of hypoglycemia, dizziness, weakness, and drowsiness were the ones known to most patients and headache and seizures, the least. Hypoglycemia may manifest with any symptom, and common symptoms may not always be the first to appear. Therefore, the patients must be aware of every symptom in order to recognize early and take immediate corrective measures.

Missing meals as a precipitating factor was known to two-thirds of the patients and exertion to a third of the patients only. It is very important that the patients are well aware of the precipitating factors/causes so that they may take appropriate precautions such as taking toffees or packed food before planning to travel or exercise. Only a third of the patients had knowledge on the complications, and <50% knew that they have to report such episodes to the doctor. Awareness about the complications would induce the patients to take this condition seriously and report any such episodes to the physician immediately.

Even though 85% of the study population are diabetic for more than 5 years, Self-Monitoring of Blood Glucose (SMBG) as a way to prevent future episodes was known to a fifth of the patients only. It is well-known that SMBG aids in better glycemic control and prevention of hypoglycemia in diabetes patients by allowing for adjustments in diet, physical activity, and pharmacotherapy in response to test results. , In this study, the knowledge on hypoglycemia decreased as age increased. This finding is shown in other studies too. This might have been because of age-related cognitive decline insisting the importance of periodical educational programs to reinforce their knowledge.

Among the participants 49% preferred taking glucose powder or sugar dissolved in water as an immediate measure for their hypoglycemic symptoms. Majority (65%) felt going to hospital emergency department was the right option for immediate management of Hypoglycemia. The more literate the patient was, he could identify symptoms of hypoglycemia and take corrective measures to avoid severe hypoglycemia. A study conducted in England among Type-2 diabetes, 5.9% patients on



OHA's in the age group of 40 to 65 years experienced hypoglycemic symptoms. None of these patients required hospitalization as they aware on the immediate management of hypoglycemia as they received good diabetic education. Ya-Chun et al studied 1195 patients with type 2 DM and observed 7.4% to have experienced severe hypoglycemia. Patients on insulin experienced hypoglycemia more frequently (17.8%) as compared to patients on OHA's (6.3%). The risk factors for developing severe hypoglycemia were older age, lower literacy level and insulin therapy. Zammitt NN and Frier BM observed an increased risk of hypoglycemia among older adults and those with diabetes for many years.

The immediate treatment of hypoglycemia should be known by all the diabetic patients, so that need for hospitalization could be avoided. Illiterate patients and elderly patients with dementia must be more educated about hypoglycemia. Thus improving patient skills self-management, self-monitoring of sugar and adjustments of dose based on requirements can reduce the risk of hypoglycemia. Severe hypoglycemia is usually associated with increased mortality, impaired cognitive function and affects patient's quality of life. Frequent hypoglycemic spells can burden the existing healthcare facilities and productivity at workplace can be affected.

This study emphasizes the role of health care workers-doctors, nurses, diabetes educators, lab technicians in providing health education to the patients during every visit. They must educate on target levels, importance of SMBG, symptoms of hypoglycemia, the ways of preventing it and immediate remedial measures to be adopted during every visit. Furthermore, periodical educational reinforcement programs need to be conducted for all diabetic patients which must include topics on hypoglycemia.

This is one of the few studies in India to study exclusively about the knowledge on hypoglycemia in detail among the type 2 diabetic patients. In India, which has the second largest number of diabetes patients, there is negligible data on the epidemiology of hypoglycemia. The limitation of the study is that the knowledge is assessed among patients

attending a diabetes free Clinic in a tertiary care hospital and may not be accurately representing that in a community comprising both affordable and poor patients.

### Conclusions

Although the knowledge on the symptoms, remedial measures, and prevention of hypoglycemic episodes was good among the type 2 diabetic patients in the study, there were gap in knowledge on important aspects like precipitating factors, target levels etc., which need to be addressed by health care workers through regular educational programs.

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Case Report



## Response to Cabergoline treatment in Invasive Prolactinoma with hemorrhage- A case report

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### Abstract

Patients with invasive prolactinoma present with constellation of symptoms including headache, blurred vision, lethargy, menstrual irregularity and sexual dysfunction. Cabergoline, a potent dopamine agonist, is a known medication prescribed for the treatment of prolactinoma. Here, we report a case of invasive macroprolactinoma with hemorrhage in a 18 years female with dramatic response to cabergoline treatment clinically, biochemically, and radiologically.

**Keywords :** cabergoline; prolacti ; prolactinoma

### INTRODUCTION

Pituitary adenomas are benign tumors of the pituitary gland, with lactotroph cell adenoma (prolactinoma) being the commonest, accounting for 44% of known cases.<sup>1</sup> Microprolactinomas are less than 1 cm in diameter whereas macroadenomas measures more than 1 cm.<sup>1</sup> Invasive giant macroadenoma are defined as tumor size above 4 cm and serum prolactin more than 1000 ng/mL with clinical symptoms of hyperprolactinemia or mass effect. Prolactinomas come to attention because of the effect of the elevated prolactin on the reproductive system and/or due to the compression effect of the tumor.

Dopamine agonists reduce the size of prolactinomas by inducing a reduction in cell volume via inhibition of secretory mechanism as well as causing perivascular fibrosis and cell necrosis.<sup>2</sup> It has been demonstrated that cabergoline is safe and effective for treatment of invasive giant prolactinomas, even when administered in relatively high doses for longer duration.

In this case, we describe the case of a 18 years Nepalese female diagnosed with macroprolactinoma with hemorrhage and its dramatic response to dopamine agonist (cabergoline).

### CASE REPORT

Eighteen years old female from kathmandu presented to the endocrinology OPD of Tribhuvan university teaching hospital on 26th January 2016 with complains of headache and decreased bilateral vision for 3 months. She also had generalized fatigability, lethargy and menstrual irregularities for 2 years. She also reported history of galactorrhea on and off. There is no history of hearing loss, abnormal movements of body or altered level of consciousness. Family history was unremarkable.

On physical examination, patient was conscious. Vital signs were stable. Thyroid examination was normal. Perimetry examination showed bilateral superior quadrantanopia with full range of extra ocular muscle movements. Systemic examination was unremarkable. Laboratory investigations showed hyperprolactinemia. Initially, serum prolactin was >320 ng/mL. Then after 200 times dilution serum prolactin value was 49,680 ng/mL (normal value = 3-18.6 ng/mL). Other pituitary work-up was normal. Serum cortisol at 8 a.m and overnight dexamethasone suppression test were within normal range. There was no finding suggestive of hypogonadism, hypothyroidism, and adrenal insufficiency. Plain Magnetic resonance imaging (MRI) of head was done which revealed a mass of 2.2

\* 1.5 cm within the pituitary fossa. Mass was extending superiorly and compressing optic chiasma. High signal intensity was noted due to hemorrhage (Fig. 1). The patient was thus diagnosed with pituitary macroadenoma with hemorrhage. She was then started on cabergoline 0.25 mg twice weekly and was advised to follow up after one month with laboratory reports of serum prolactin.

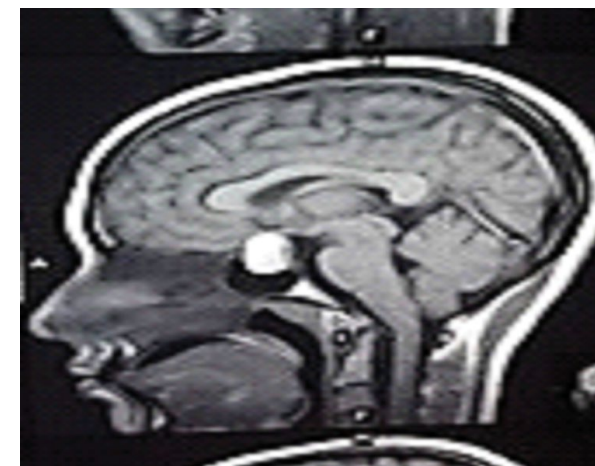


Figure 1. Pituitary macroadenoma with hemorrhage

After one month on 4th March 2016, serum prolactin levels dropped to 1152.0 ng/mL (3-18.6 ng/mL), with subsequent improvements in vision and headache. Perimetry test showed normal results. The patient was then prescribed with higher dose of cabergoline 1.25 mg twice a week and was advised to follow up after 3 months. Gradually her serum prolactin dropped down to high normal range after one and half year of treatment. She regained her normal menstrual cycle. On 31st July 2017, her serum prolactin was 19.0 ng/mL and her repeated MRI of brain with pituitary showed complete disappearance of pituitary lesion as compared to earlier imaging (Fig. 2).



Fig 2. Normal Pituitary MRI after one and half years of treatment

### DISCUSSION

Treatment of invasive giant prolactinoma with locoregional spread and visual field compromise using cabergoline has been observed to provide excellent outcomes. Our case illustrates the efficacy of cabergoline in treating invasive macroprolactinoma with hemorrhage and reversing patient's symptoms.

In female, prolactinoma is usually diagnosed earlier than men because of presence of menstrual disturbances due to hyperprolactinemia. Macroadenoma compresses pituitary stalk causing loss of dopamine inhibitory tone to the lactotroph and subsequent hyperprolactinemia. Our patient had initially presented with irregular menses in various hospitals but her symptoms were overlooked. Finally she presented to us with visual disturbances and headache.

In our case, serum prolactin was more than 320ng/mL during her first visit to us. After dilution of the sample, serum prolactin value was 49,680 ng/mL. The Endocrine Society's



Clinical Guideline "Diagnosis and Treatment of Hyperprolactinemia" in 2011 recommends that in case of discrepancy between a very large pituitary tumor and a mildly elevated prolactin level, serial dilution of serum samples need to be performed to eliminate an artifact leading to a falsely low prolactin value the so called "hook effect" or high dose hook (HDH) effect.<sup>3</sup>

Significant improvements were observed in our case after an initial dose of 0.25 mg of cabergoline twice weekly. Also, patient showed dramatic improvement in visual field symptoms within the first month of therapy. Her menstrual cycle was normal after one and half years of treatment. During this period her serum prolactin was near normal. Various cases has been reported where treatment with cabergoline for 18 months markedly reduced tumor size and visual field improvement.<sup>4,5</sup> Transsphenoidal surgery is indicated only for patients who are resistant to dopamine agonist treatment.<sup>6</sup> Also, the cure rate for macroprolactinoma and microprolactinoma treated with surgery is poor which is 30% and 80% respectively and there is a risk of hypopituitarism and recurrence.<sup>6</sup> Occasionally, surgery may be required for patients with CSF leak. Cabergoline is more effective than other dopamine agonist like bromocriptine in normalization of serum prolactin in pituitary microadenoma. This case reinforces the effectiveness of cabergoline treatment and emphasizes the potential reversibility of pituitary function in patients harboring invasive and aggressive prolactin-secreting pituitary tumors with hemorrhage. This case also supports medical treatment over surgery for prolactinomas

and demonstrates that cabergoline is a safe and effective treatment and should be recommended as a first line therapy.

### CONCLUSIONS

Cabergoline has been successfully used in treatment of invasive giant prolactinoma. This case supports medical treatment over surgery for prolactinomas with hemorrhage.

### CONFLICT OF INTEREST

Authors declare that there is no conflict of interest in the publication of this case report.

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## Journal of Diabetes and Endocrinology Association of Nepal

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