



## PRESCRIPTION PATTERN OF INSULIN, FREQUENCY OF HYPOGLYCAEMIA IN PATIENTS WITH DIABETES MELLITUS IN A TERTIARY CARE CENTRE-A SHORT TERM PILOT STUDY.

<sup>1</sup>\*Dr. Bezawada Shravani, <sup>2</sup>Dr. Anuradha HV, <sup>3</sup>Dr. Pramila Kalra.

<sup>1</sup>Post Graduate. Dept. of Pharmacology. MS Ramaiah Medical College, Bangalore, India.

<sup>2</sup>Professor of Pharmacology, MS Ramaiah Medical college.

<sup>3</sup>Professor of Endocrinology, MS Ramaiah Medical college.

Article Received on  
24 March 2017,

Revised on 13 April 2017,  
Accepted on 03 May 2017

DOI: 10.20959/wjpps20176-9248

**\*Corresponding Author\***

**Dr. Bezawada Shravani**

Post Graduate. Dept. of  
Pharmacology. MS Ramaiah  
Medical College, Bangalore,  
India.,

### ABSTRACT

**Background:** Diabetes Mellitus (DM) is a metabolic disorder characterised by prolonged hyperglycaemia due to inadequate insulin secretion or defective insulin action or both. Oral hypoglycaemic agents (OHAs) and insulin are treatment of choice for DM. Hypoglycaemia in diabetes is defined as blood glucose < 54 mg/dl (3.0 mmol/L), while the glucose alert value is defined as < 70 mg/dl (3.9 mmol/L) presenting as giddiness, sweating and shivering. **Aim and objectives:** To study the prescription pattern of insulin and frequency of hypoglycaemia in diabetic patients and its incidence with different types of insulin. **Methods:** A cross sectional study was done over a

period of 2 months on 30 diabetic patients (type1 & 2) >18yrs of age, who were on insulin regularly and willing to participate with written informed consent. Patients receiving single or multiple injections of insulins with/without OHA's were assessed. Overall the number of patients having symptomatic hypoglycaemia and its frequency with single or multiple injections of insulins were assessed. **Results:** Out of 30 diabetic patients included in the study, 60% of patients were prescribed with single insulin therapy and 40% with multiple insulins. Seventy two percent of patients prescribed with single insulin were taking inj. premix 30/70. The most commonly prescribed insulin in combination therapy were that of isophane and regular insulins and least with combination of Glargine and regular insulins. Overall 67% of the patients presented with mild hypoglycaemic symptoms and were treated at home accordingly. **Conclusion:** Multiple preparations and combinations of insulins are

being prescribed in DM patients. Conventional insulins show more hypoglycaemia as compared to insulin analogues.

**KEYWORDS:** Prescription, Insulin, Diabetes, Hypoglycaemia.

## INTRODUCTION

Diabetes Mellitus (DM) is a metabolic disorder characterised by prolonged hyperglycaemia due to inadequate insulin secretion or defective insulin action or both.<sup>[1]</sup> The total number of people with diabetes is approximated to rise from 171 million (2000) to 366 million in 2030.<sup>[2]</sup> Oral hypoglycaemic agents (OHAs) and insulin are treatment of choice for DM. Hypoglycaemia in diabetes is defined as glucose < 54 mg/dl (3.0 mmol/L), while the glucose alert value is defined as < 70 mg/dl (3.9 mmol/L) presenting as giddiness, sweating and shivering.<sup>[1]</sup> The number of individuals with diabetes is rapidly raising. Genetic and environmental factors could contribute to its pathogenesis.<sup>[3]</sup> Diabetes is mainly classified as type 1 diabetes (insulin dependent), type 2 diabetes (non-insulin dependent) and gestational diabetes.<sup>[4]</sup> In type 1 diabetes the islets beta cells are destroyed by an autoimmune process so that the insulin synthesis is reduced and it is less common. Type 2 DM are mainly because of several causes such as relative insulin deficiency (deficiency insulin for increased metabolic needs), insulin resistance and hyperinsulinaemia.<sup>[2]</sup>

Retinopathy, neuropathy, nephropathy, and cardiovascular disease are the major complications associated with diabetes.<sup>[3]</sup> Many oral hypoglycaemic agents like sulfonylureas, meglitinides, biguanides and alpha glucosidase inhibitors are being prescribed routinely. The newer drugs like Dipeptidylpeptidase4 (DPP4) inhibitors, glucagon like peptide, sodium glucose transporter inhibitors are having better efficacy and upcoming in the market for prescription. Insulin is the mainstay for treatment of virtually all type 1 and many type 2 diabetes patients. Insulin can be administered intravenously, intramuscularly, or subcutaneously however subcutaneous injection is preferred route of administration for long term therapy.<sup>[3]</sup> Insulin preparations are classified in ultra-short, short, intermediate and long acting.<sup>[5]</sup> The newer insulin are obtained by recombinant DNA based technology with modified pharmacokinetic profile but with similar Pharmacodynamic effects like conventional insulins provide and hence newer insulin analogues are more stable and consistent. These are either given as mono-therapy or combination regimen.<sup>[5]</sup>

Adverse effects like hypoglycaemia, itching, lipodystrophy, rash etc., due to these insulin and anti-diabetic drugs needs to be understood.<sup>[5]</sup> Proper and appropriate insulin administration can prevent many of the adverse outcomes associated with hyperglycaemia. There is inadequate information with respect to patient education on proper glucose monitoring and optimisation of insulin therapy. Studies have shown the prescription pattern of anti-diabetic medication overall in type 2 diabetes mellitus.<sup>[6, 7, 8]</sup> It is important to understand the different preparations of insulin and adverse reactions like hypoglycaemia and modify the dose based on patient needs.

### **AIM & OBJECTIVE**

To study the prescription pattern of insulin in diabetic patients.

To assess the frequency of hypoglycaemia in diabetic patients on insulins with or without oral hypoglycaemic agents (OHAs)

### **MATERIALS & METHODOLOGY**

A cross sectional pilot study was conducted at MS Ramaiah Hospitals. Thirty diabetic patients above the age of 18yrs, both type 1 & 2 attending the outpatient department of Endocrinology were studied. The duration of the study was from April 2016 to May 2016. A written informed consent was obtained from the patient prior to the study and the study was ethically approved. Demographic parameters like age, gender, education, height weight were noted. The prescriptions of these patients were studied. Insulin -types, regimens, dose, route, frequency were noted. The various oral hypoglycaemic agents their dose, frequency, duration were too noted. Concomitant medications for comorbidities were noted from the prescription. A set of question with regards to adverse effects after consumption of insulin were asked to the patients. Patients prescribed with insulin solely or in combination. With oral hypoglycaemic agents were noted. Frequency of hypoglycaemia with respect to medications prescribed –insulin with/without OHAs was assessed.

### **INCLUSION CRITERIA**

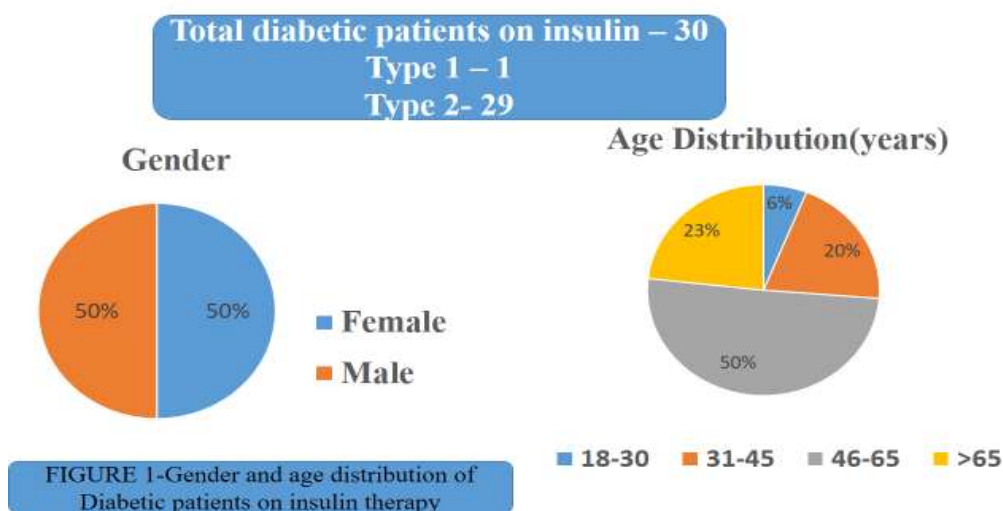
Diabetic patients type 1 & 2, above the age of 18yrs, on insulin therapy and willing to give informed consent were included in the study

### **EXCLUSION CRITERIA**

Pregnant and lactating Diabetic mothers

## RESULTS

After analysing the various insulin preparations, doses, frequency and schedules either with or without oral hypoglycaemic agents the results were tabulated accordingly. Thirty diabetic patients' prescription patterns were assessed. Figure 1 shows that majority of patients were of type 2 diabetes mellitus of the age group between 46-65 years. Ninety seven percent of patients presented with type 2 diabetes and 4% were belonged to type 1 diabetes.



In figure 2 fifty six percent of the patients also had most common presentation of hypertension and primary hypothyroidism as comorbid conditions.

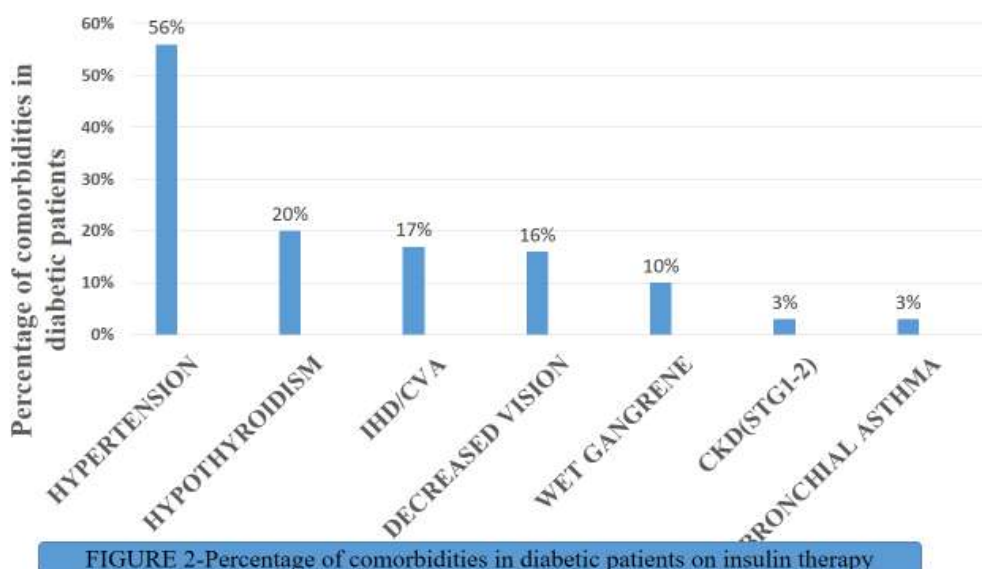


Figure 3 shows that most of the patients were on insulin monotherapy (60%) with oral hypoglycaemic agents.

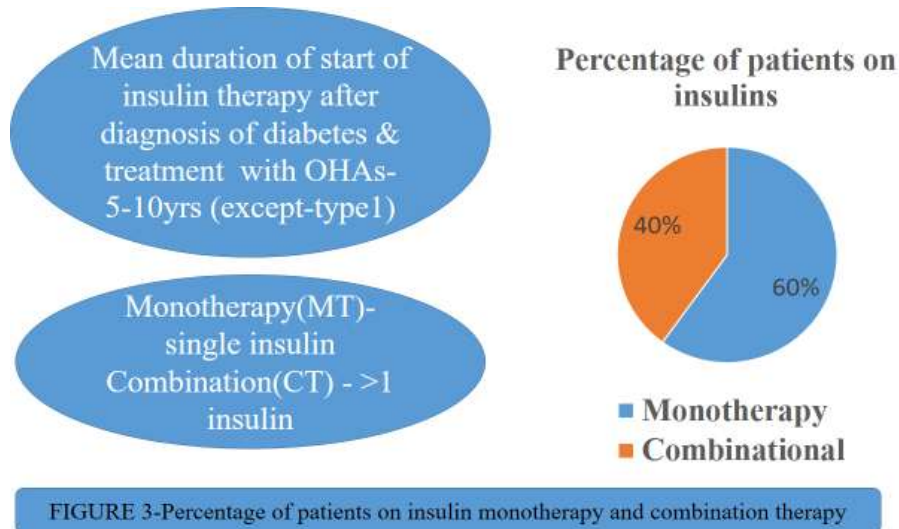
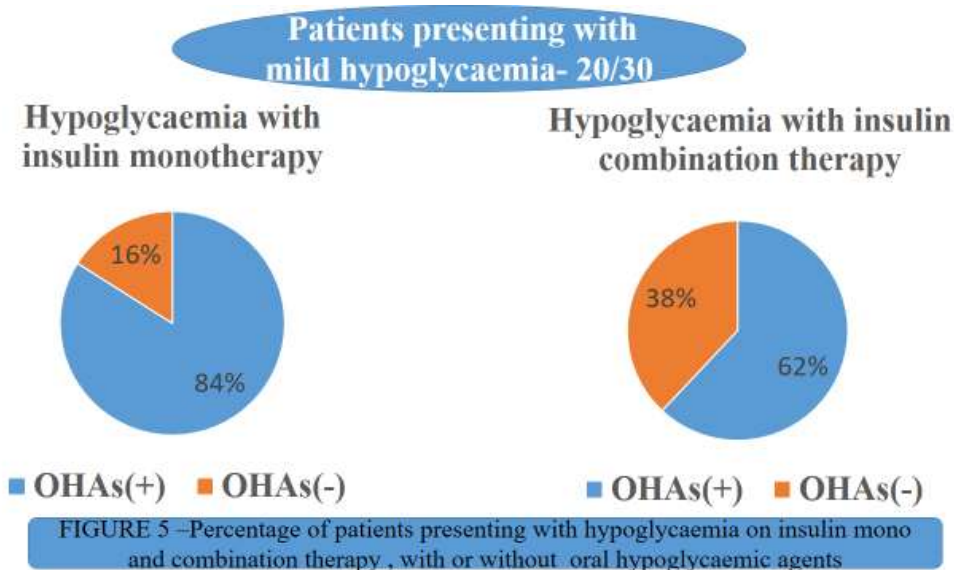
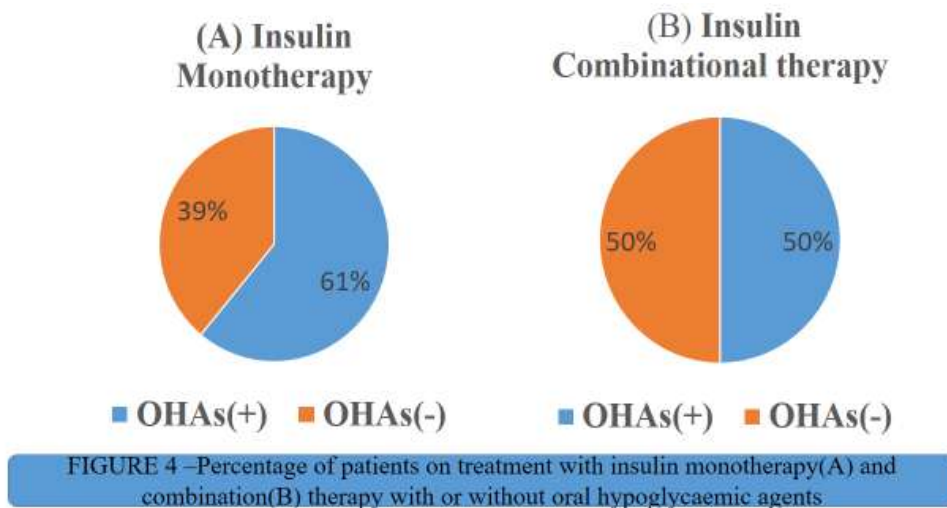


Figure 4 shows that 61% of patients were on insulin monotherapy and 50% each with or without OHA'S in combination therapy.



In figure.5, more than two third of the patients (84%) presented with hypoglycaemia as most common adverse drug reaction after taking insulin and oral hypoglycemics together.

Hypoglycaemia was most commonly seen in patients who took intermediate insulins as shown in figure 6. This was most commonly with seen with inj.premix followed by regular insulin and very less with newer insulin analogues like insulin.aspart.

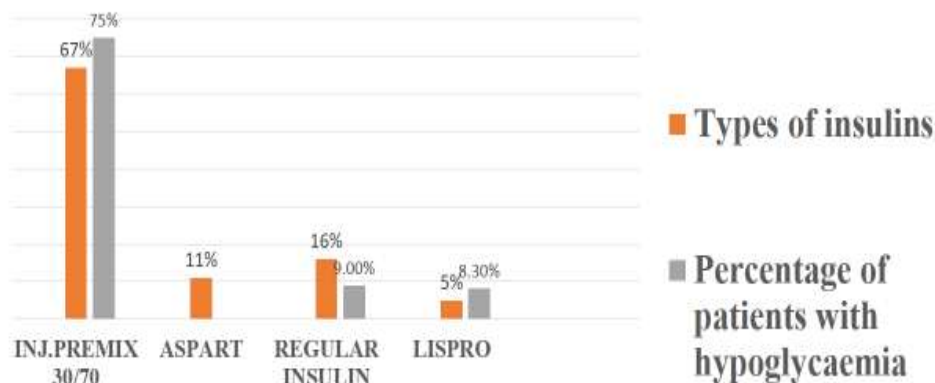
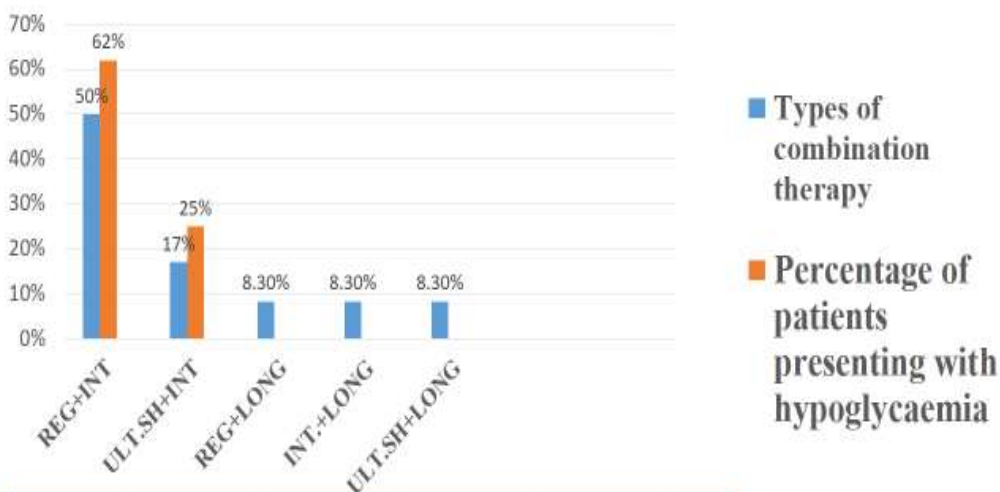


FIGURE 6 – Percentage of patients with hypoglycaemia prescribed with various types of insulin

In figure 7 the insulin induced hypoglycaemia was more commonly seen with combination of regular and intermediate insulins (62%) followed by ultra short acting and intermediate acting combination of insulins (25%).



1. REG- REGULAR 2. ULT.SH- ULTRASHORT 3. INT.-INTERMEDIATE

FIGURE 7-Percentage of patients with hypoglycaemia in insulin combination therapy

## DISCUSSION

Diabetes mellitus is non communicable, metabolic disorder characterised by hyperglycaemia, glycosuria, hyperlipidaemia, negative nitrogen balance and sometimes ketonaemia.<sup>5</sup> There is thickening of capillary basement membrane and cellular proliferation.<sup>[5]</sup> It is one of the most prevalent disease in the present era and is going to hit many lives in near future due to trending lifestyle currently. It is global burden which needs to be addressed. Variety of drugs are being used in and out for control of hyperglycaemia along with non-pharmacological methods like life style changes, exercise, diet control etc. Insulin is the best medication in the current era prescribed for achieving adequate glycemic control at the earliest possible with minimal adverse drug reaction. As insulin is an injectable preparation on regular basis, non-compliance was the most common complaint expressed by the patients.<sup>[6]</sup>

A total of 30 patients were enrolled in the current study. The prevalence of DM in our sample population was found to be equal in both males and females. These results however cannot predict the exact reason behind this kind of distribution. The sample largely belonged to group of both rural population and urban population. Majority of the study population, approximately about 50% belonged to the age group of 46-65 years. Ninety seven percent of patients presented with type 2 diabetes and 4% were belonged to type 1 diabetes. Patients suffered from various comorbid conditions like hypertension, decreased vision, ischaemic heart disease, diabetic foot ulcers, gangrene etc. Hypertension followed by primary hypothyroidism were the most common comorbid conditions in majority of the patients.

Mean duration of start of insulin therapy for most of the patients was 5yrs after the onset of diabetes which makes one to note that diabetes is a progressive disease and as it progresses with increasing age, the body requires stricter glycaemic control. The oral hypoglycaemic agents mostly prescribed along with insulin mono-therapy were metformin and sulfonylureas-glipizide, gliclazide. In a study conducted by Camilo Molino Guidoni et al glibenclamide, metformin was prescribed with insulin mono-therapy.<sup>[9]</sup> Sixty percent of the patients were on insulin mono-therapy (single) in the present study. Dosing schedule of insulin was ranging from one to four times daily. This was similar to the study conducted by Ogbera and Kuku et al.<sup>[9]</sup> The most common route of administration was subcutaneous and before meals with timing based on the preparation of insulin being administered.

Twenty patients (67%) complained of giddiness, sweating, hypoglycaemic like symptoms after administration of insulin. These symptoms were more commonly seen when insulin (monotherapy/combination) was given in combination with that of oral hypoglycaemic agents. These symptoms were mild to moderate in intensity and were treated at home by consumption of glucose based foods etc. Inj. premix was the most common prescription when given as a monotherapy followed by ultra-short, short and long acting insulin. Regular insulin with intermediate acting insulin were the most commonly prescribed combination regimens and hypoglycaemia was seen with this combination as when compared to the combination of long and intermediate or long and short/ ultra-short acting insulins.

Medications were prescribed based on blood glucose levels and body weight. Both insulin analogues and conventional were cost effective and achieved good glycaemic control equally with good compliance. Hypoglycaemia was seen more commonly in conventional insulins as compared to analogues. One patient even presented with itching and mild rash on the skin at the injection site. In a study conducted by Nikky Jain Thomas *et al.*<sup>[6]</sup> majority of the patients 109(90.83%) were prescribed with Human Actrapid and 11(9.16%) patients were prescribed with Human premix. A similar study was conducted in Sree Ramachandra University involving 350 patients, revealed that 248(70.8%) were found to be administered with Human premix.<sup>[6]</sup>

This makes one to understand that intermediate acting insulins are the most needful by the patients and are compliant in nature however a combination of long acting and ultrashort acting could also provide adequate glycaemic control. In primary and secondary health care centres long and intermediate conventional insulins with first generation sulfonylureas are being prescribed more which could lead to worsening of cardiovascular profile of patients, whereas in tertiary care centres long acting and short acting insulin analogues along with conventional insulins and second generation sulfonylureas are being prescribed which favours the cardiovascular effects of patients. Newer analogues seem to be safer. The limitation of this study it is a pilot study and done on fewer patients and in depth analysis of blood glucose levels in relation with the dosing of insulin needs to be up taken in upcoming studies for optimum control of glycaemic levels.

## CONCLUSION

This study educates one to understand about the various pharmacological therapies for diabetes mainly focussing upon preparations of insulins and the frequency of hypoglycaemia



associated with its use. Conventional insulins are known to cause more hypoglycaemia (mild) when compared to analogues. However there is a need for optimum, vigilant monitoring and reporting of hypoglycaemic episodes due to insulin therapy in larger diabetic populations in future for the betterment of health.

### **FUTURE STUDY**

Prescription studies of insulin and their adverse drug reaction monitoring need to be done on larger diabetic population and follow up studies needs to be undertaken.

### **ACKNOWLEDGEMENT**

We sincerely thank our patients at MS Ramaiah Hospitals who cooperated for successful completion of this short term pilot study.

### **REFERENCES**

1. Wild S, Roglic G, Green A, Sicree R, King H. Green A et al. "Global Prevalence Of Diabetes: Estimates For The Year 2000 And Projections For 2030". *Diabetes Care* 27.5, 2004; 1047-1053. Web. 25 Apr. 2017.
2. Standards of Medical Care in Diabetes 2017: Summary of Revisions *Diabetes Care*, 2017; 40(Suppl. 1): S4–S5 | DOI: 10.2337/dc17-S003. [Cited on 25 April 2017]
3. Goodman L, Gilman A, Brunton L, Lazo J, Parker K. Goodman & Gilman's the Pharmacological Basis of Therapeutics. 12<sup>th</sup> edition, New York; McGraw-Hill, 2006; 1153-1156.
4. Masters S, Trevor A. Basic and clinical Pharmacology. 13<sup>th</sup> edition, McGraw-Hill, 2015, 1417.
5. Tripathi KD. Essentials of medical pharmacology. 7<sup>th</sup> edition, Jaypee Brothers, 2013; 258-261.
6. Thomas NJ, K.R H, Abraham A, Pandey M et al. Study of Prescription Pattern of Insulin in Diabetic Patients in A Tertiary Care Teaching Hospital. *Indo American Journal of Pharm Research*, 2015; 5(06).
7. K V H, R R, Thomas N, Raghu R et al. Study of prescription pattern and insulin treatment in type 2 diabetic patients *Int J pharm pharm sci*, 2012; 4(3): 328-330.
8. Ogbera AO, Kuku SF. Insulin use, prescription patterns, regimens and costs-a narrative from a developing country. *Diabetology & Metabolic Syndrome*, 2012; 4: 50.

9. Guidoni CM, Borges AP, Frieda Od, Pereira LR et al .Prescription patterns for diabetes mellitus and therapeutic implications: a population-based analysis. *Arq Bras Endocrinol Metab*, 2012; 56/2.
10. Frier B, Jensen M, Chubb B. Hypoglycaemia in adults with insulin-treated diabetes in the UK: self-reported frequency and effects. *Diabetic Medicine*, 2015; 33(8): 1125-1132.