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A COMPARITIVE STUDY ON INCIDENCE AND FREQUENCY OF HYPOGLYCEMIC MANIFESTATIONS IN PATIENTS WITH UNCONTROLLED TYPE 2 DM WITH AND WITHOUT COMPLICATIONS AT A TERTIARY CARE HOSPITAL

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ABSTRACT

Objective: To compare the incidence of hypoglycemic manifestations in uncontrolled type 2 DM with and without complication. To identify the frequency of hypoglycemia in uncontrolled type 2 DM patients with and without complication. To assess the hypoglycemic manifestations using Naranjo causality assessment scale. Subjects with uncontrolled type 2 DM (n=101) were included in the analysis. If the patient showed any clinical manifestations in that instant gross random blood sugar was taken and confirmed hypoglycemia. P value of FBS and GRBS to be calculated by Graph pad prism version 8.4.0 (671). Distribution of uncontrolled type 2 DM with complication is (34.65%) and uncontrolled type 2 DM without complication is (65.34%). Male (55.45) gender is more susceptible to uncontrolled type 2 DM than female gender (44.55). The age group between 50-59 of uncontrolled type 2 DM with complication (31%) and uncontrolled type 2 DM without complication (30.6%). FBS of ≤70mg/dL to be noted and p value is 0.034. GRBS of ≤70mg/dL to be noted and p value is 0.047. Nephropathy (37.14%) is major complication in uncontrolled type 2 DM with complication. Incidence of hypoglycemia in uncontrolled type 2 DM with complication (51.42%) and in uncontrolled type 2 DM without complication (34.84%).only one episode of hypoglycemia occurred in both uncontrolled type 2 DM with complication (50%) and uncontrolled type 2 DM without complication (60.86%).clinical manifestations of hypoglycemia varies with patient to patient. Hypoglycemia in uncontrolled type 2 DM with complication caused by insulin (50%) and in uncontrolled type 2 DM without complication caused by OHA (52.17%).On assessing the ADR (hypoglycemia)in uncontrolled type 2 DM with complication is definite(77.77%) and in uncontrolled type 2 DM without complication also definite (65.21%).

KEYWORDS: Uncontrolled type 2 diabetes mellitus, complications, incidence, frequency , clinical manifestations of hypoglycemia.

INTRODUCTION

Uncontrolled type II diabetes mellitus also known as non-insulin dependent diabetes mellitus characterized by the defective secretion of insulin and increased insulin resistance or reduced insulin sensitivity. Distinctive feature of uncontrolled type 2 diabetes mellitus is the persistently elevated blood glucose level, even though the patient is under regular medication. In 1998 it was estimated that, globally, there were already 140 million people with diabetes. Predictions compiled by Dr. Hilary King of the World Health Organization indicate that this figure will rise to 300 million by the year of 2025. Figures for India are predicted to rise from an estimated 15 million in 1995 to 57 million in 2025. In 2015, adults aged 45 to 64 were the most diagnosed age group for diabetes.[1]

Hypoglycaemia is the reduction in blood glucose level less than or equal to 70mg/dl. Various etiological factors leading to hypoglycaemia are intense hypoglycaemic therapy/ higher dose, alcoholism, liver complications, skipping meals, heavy exercise and older age. Hypoglycaemia triggers a stress condition to the body and attempts made by the body to overcome such situation manifests as the warning signs and symptoms of the hypoglycaemia. Early adrenergic symptoms are the first to manifest during hypoglycaemia. They consist of diaphoresis, tremor, hunger, anxiety, irritability, headache and dizziness. Later neuroglycopenic symptoms manifests when hypoglycaemia continues and symptoms such as confusion slurred speech, uncontrolled behaviour, extreme fatigue, loss of consciousness, seizure, pupillary changes and decreased response to noxious stimuli.[2]

It is the only study that should be comparing the hypoglycaemic manifestations in uncontrolled type 2 DM with complication and without complications.

METHODOLOGY

The study was designed to be a Prospective Interventional Study, Conducted in Karuna Medical College Hospital (KMCH) for a duration of 6 months (October 2019 to March 2020) and was carried out in inpatient department from General medicine, Surgery ward and Special ward. A total of 101 patients enrolled in the Study. The study protocol was approved by Institutional Ethics Committee SDAT/KMC/EC/12-2017/86.

INCLUSION CRITERIA

Patient of both sex with age ≥ 30 years. The patient who are diagnosed with uncontrolled type II DM with and without complications and admitted in general medicine, surgery, Causality and special ward.DM complication includes nephropathy, neuropathy, cardiovascular complications and diabetic foot ulcer.

EXCLUSION CRITERIA

Patient diagnosed with type I DM, gestational diabetes and diabetic retinopathy. Outpatients diagnosed with all types of DM. Patients who are not willing to sign the consent form or cooperative. Severely ill patients admitted in ICU and having any type of malignancy.

STATISTICAL ANALYSIS

Data were sorted and percentage were calculated by using Microsoft excel 2019.

Graph pad prism version 8.4.0(671) used to analyse the FBS and GRBS by unpaired t-test.

RESULT AND DISCUSSION

figure:1 showed distribution according to uncontrolled type 2 DM with complication and without complication. Out of 101 uncontrolled type DM patients, about 34.65% (n=35) were with complication and about 65.34% (n=66) were without complication. In contrast to our study, Alabound AF *et al.* concluded that Both macrovascular and microvascular complications are more prevalent in type 2 DM. Because high blood sugar can damage both tiny and large blood vessels which causes macrovascular and microvascular complications.

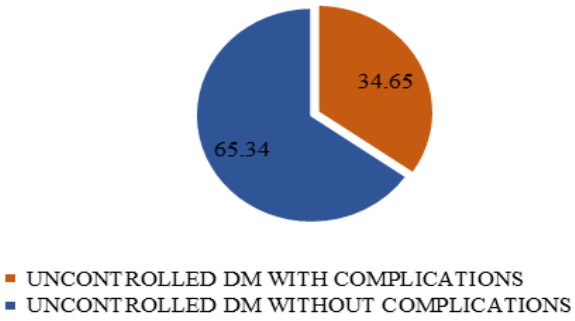

Figure 1: Distribution based on complications of uncontrolled DM among the population.

Figure:2 showed the distribution of uncontrolled type 2 DM according to gender. Male gender (55.45%) is more susceptible to uncontrolled type 2 DM than female gender (44.55%). Similarly, study conducted by Rombopoulous *et al.* also found higher occurrence of type 2 DM in males comparing with females. Because men having large amount of visceral fat.

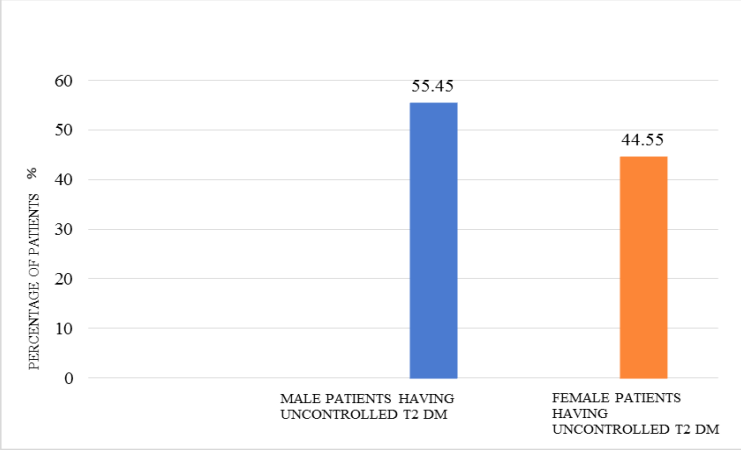

Figure 2: Distribution based on Gender.

Table:1 showed distribution of patients according to age group between 50-59 (30.6%) and 60-69 (29%) are more prone to uncontrolled type 2 DM. Similarly, K Haritha *et al.* also concluded that subjects about age 50-59 are more prone to type 2 DM. This is due to age related decline in pancreatic β- cell function[3]

Table 1: Distribution based on Age.

Sl. No	Age In Years	Number Of Patients(n=101)	Percentage (%)
1	30-39	3	2.97
2	40-49	16	15.8
3	50-59	31	30.6
4	60-69	29	28.7
5	70-79	17	16.8
6	80-89	5	4.95
	MEAN AGE IN YEARS	60.04±11.7	

Table:2 showed distribution based fasting blood sugar performed among study population. In uncontrolled type 2 DM. FBS ≤70 mg/dL, mean FBS was found to be 50.55 and SD(12.57).In uncontrolled type 2 DM FBS ≤70 mg/dL mean FBS was found to be 56.55 mg/dL SD (11.84).P value found to be 0.034. FBS of >70 mg/dL mean was found to be 165.95 and SD(86.81) in uncontrolled type 2 DM. In uncontrolled type 2 DM without complication mean FBS was found to be 227.3 and SD(94.81). P value found to be 0.382. In Aghazadeh M *et al.* FBS ranges from 62-492mg/dL and its mean was found to be 280mg/dL.[4]

Table 2: Distribution based on FBS performed in study population.

FBS (70-115)	Uncontrolled Type 2 DM With Complication		Uncontrolled Type 2 DM Without Complication		P -Value
	Mean	SD	Mean	SD	
≤70 mg/dl	50.55	12.57	56.06	11.84	0.034
>70 mg/dl	165.95	86.81	227.3	94.81	0.382

Table: 3, showed distribution of GRBS performed among study population. GRBS ≤70 mg/dL mean was found to be 54.42 and SD (14.91). In uncontrolled type 2 DM with complication. In uncontrolled type 2 DM without complication mean was found to be 62.61 and SD (7.48). P value found to be 0.047. Similarly, in Varghese *et al.*50% of hypoglycemia resulted in GRBS ranging from 56-60 mg/dl. GRBS<70mg/dL, in uncontrolled type 2 DM with complication, mean found to be 271.62 and SD (81.36). In uncontrolled T2 DM without complication mean was found to be 277 and SD (65). P value found to be 0.242.[5]

Tabke 3: Distribution based on GRBS performed among study population.

GRBS (70-140)	Uncontrolled type 2 DM with complication		Uncontrolled type 2 DM without complication		P Value
	Mean	SD	Mean	SD	
≤70 mg/dl	54.42	14.91	62.61	7.48	0.047
>70 mg/dl	271.62	81.36	277	65	0.242

figure:3, showed distribution according to various complication of uncontrolled type 2 DM. Nephropathy (37.14%) was found to be more with uncontrolled type 2 DM without complication. similarly, in Shih CA *et al.* nephropathy was most abundant complication. Because Microalbumin urea is the earliest sign of diabetic nephropathy. If the microalbumin urea is not detected in the early stages which will leads to impairment of kidney function.[6]

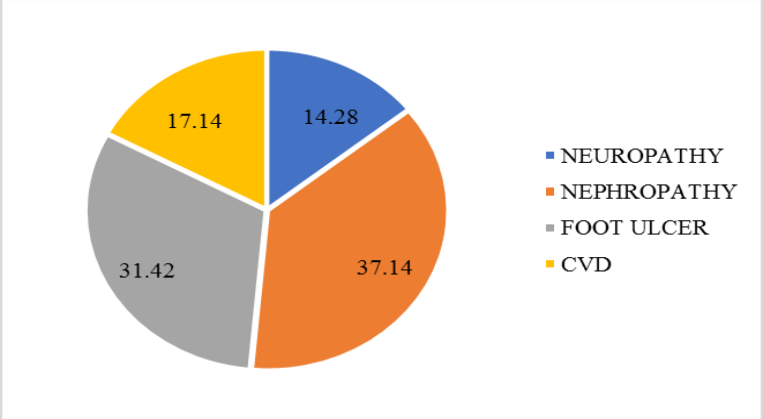

Figure 3: Distribution among various diabetic complications.

figure:4, showed distribution based on incidence of hypoglycemia in uncontrolled type 2 DM patients. Out of 45 uncontrolled type 2 DM with complication ,51.42 %show hypoglycemia. Out of 66 uncontrolled type 2 DM without complication ,34.84% show hypoglycemia. In Rombopoulous *et al.* incidence of hypoglycemia in uncontrolled type 2 DM is 22%.[7]

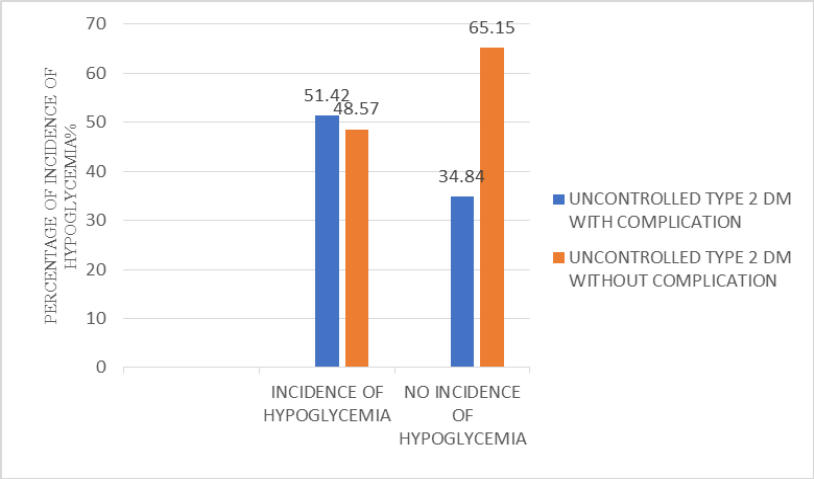

Figure 4: Distribution based on incidence of hypoglycemia in uncontrolled type 2 DM patients.

Table:4 showed distribution based on types of hypoglycemia. In uncontrolled type 2 DM with complication about 72.22% were with symptomatic hypoglycemia. Similarly, in uncontrolled type 2 DM without complication about 91.30% were with symptomatic hypoglycemia. Similarly, in Lipska KJ *et al.* Risk of severe hypoglycemia to be higher with either near or normal glycemia.[8]

Table 4: Distribution based on the types of hypoglycemia.

Types	Uncontrolled Type 2 DM With Complication		Uncontrolled Type 2 DM Without Complication	
	Number of Hypoglycemia (n=18)	Percentage (%)	Number of Hypoglycemia (n=23)	Percentage (%)
Symptomatic hypoglycemia	13	72.22	21	91.30
Asymptomatic hypoglycemia	4	22.22	1	4.34
Severe hypoglycemia	1	5.55	1	4.34

figure:5 showed distribution based on frequency of hypoglycemia. In uncontrolled type 2 DM with complication about 50% of patients shows only one episode of hypoglycemia. In uncontrolled type 2 DM without complication about 60.86% of patients show only one episode of hypoglycemia. In contrast to our study Shriram V *et al.* 2-3 times of hypoglycemic events were occurred in the study population.[9]

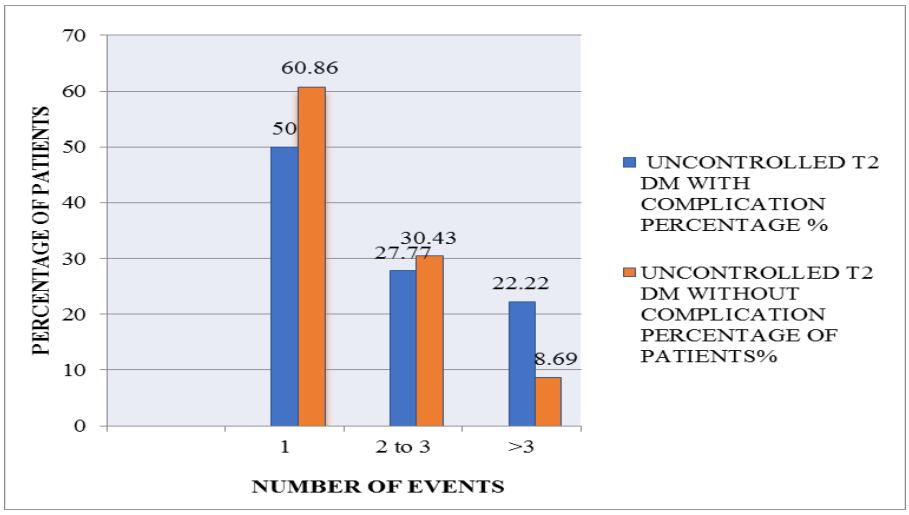

Figure 5: Distribution based on the frequency of hypoglycemia.

Table:5 showed distribution based on clinical manifestations of hypoglycemia. Both adrenergic and neuroglycopenic symptoms (66.66%) were more in uncontrolled type 2 DM with complication. Multiple adrenergic signs (52.17%) were more in uncontrolled type 2 DM without complication. In contrast to our study Asgharzadeh et al. concluded that weakness was most prominent with hypoglycemia.[10]

Table:5-Distribution of multiple clinical manifestations of hypoglycemia.

Clinical Manifestations	Uncontrolled Type 2 DM With Complication		Uncontrolled Type 2 DM Without Complication	
	Number of Hypoglycemia (n=18)	Percentage (%)	Number of Hypoglycemia (n=23)	Percentage(%)
Multiple Adrenergic Signs	4	22.22	12	52.17
Multiple Neuroglycopenic Symptoms	2	11.11	2	8.69
Both Adrenergic Signsand Neuroglycopenic Symptoms	12	66.66	9	39.13

figure:6 showed distribution based on antidiabetic medication leading to hypoglycemia.Out of 18 hypoglycemia(type 2 DM with complication) about 9 (50%) hypoglycemia caused by insulin.Similar to our study Varghese *et al*.stated that insulin will results in hypoglycemia in type 2 DM. Because insulin injections are prescribed to almost all type 2 DM patients to compensate declining insulin production by pancreas. Out of 23 hypoglycemia (without complication) about12(52.17%) hypoglycemia caused by OHA.

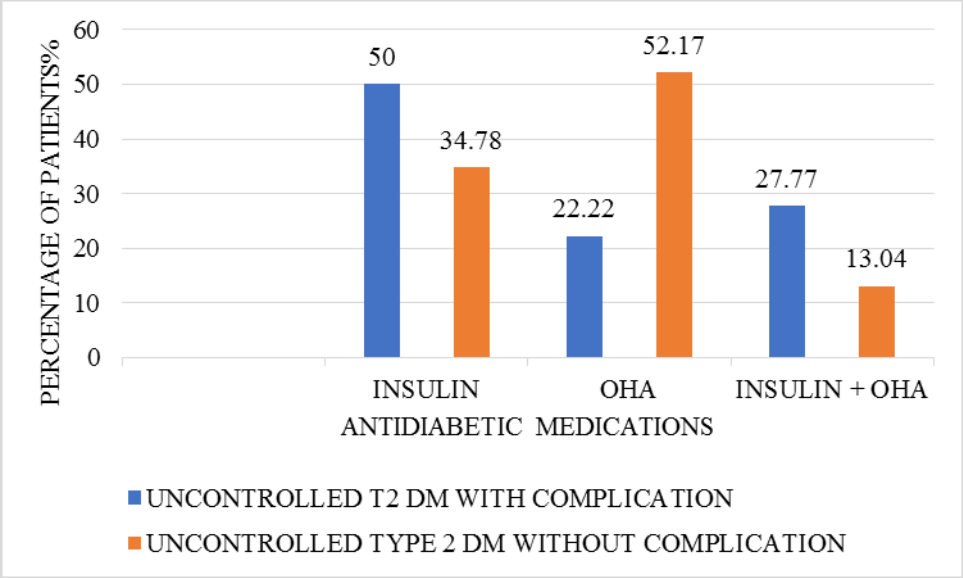

Figure 6: Distribution based on the antidiabetic medications leading to the hypoglycemia.

figure:7 showed distribution based on the hypoglycemia caused by insulin and its analogues. combination of short acting and intermediate acting insulin (66.66%) caused hypoglycemia in uncontrolled type 2 DM with complication.Short acting insulin (57.14%) caused hypoglycemia in uncontrolled type 2 DM without complication. Similarly, in Jarvinen HY *et al*.combination of short acting and intermediate acting insulin results in hypoglycemia. Because S+I combination results in higher frequency because one main function of this insulin is to control blood glucose at meal time. If you taking S+I combination without proper meal or snacks results in hypoglycemia.[11]

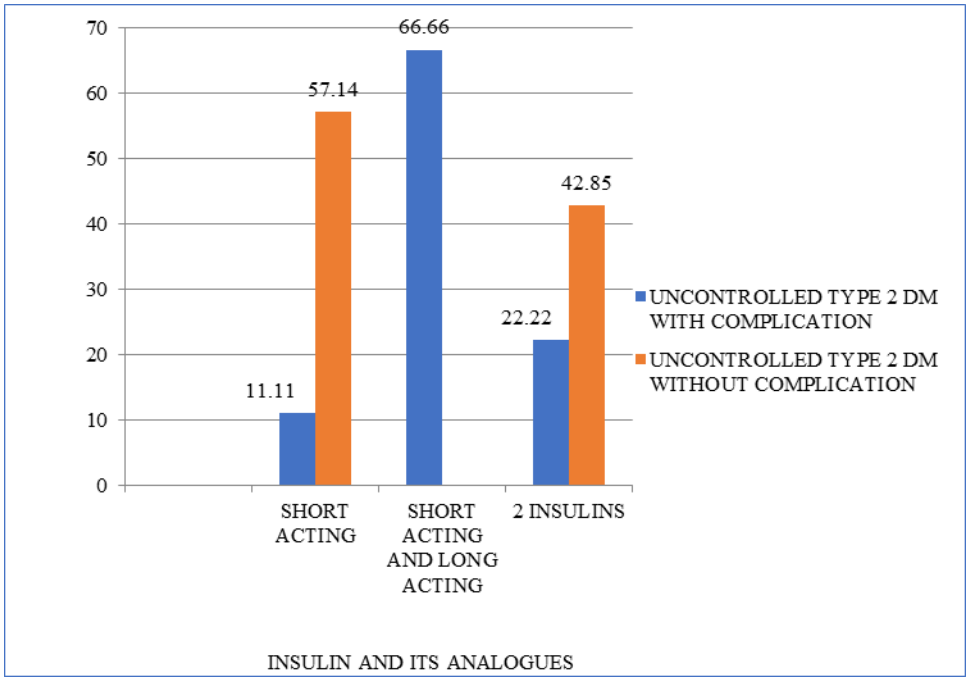

Figure 7: Distribution based on the hypoglycemia caused by the insulin and analogues.

figure:8showed distribution based on the hypoglycemia caused by OHA and insulin. Combination of Biguanides and sulfonyl urea's causedhypoglycemia both in uncontrolled type 2 DM with complication(75%) and in uncontrolled type 2 DM without complication (58.33%). similarly, in Abejew AA *etal.* combination of Biguanides and sulfonyl urea's causes hypoglycemia. Because lactic acidosis is associated with use of metformin and hypoglycemia is a major concern of using sulfonyl urea's.[12]

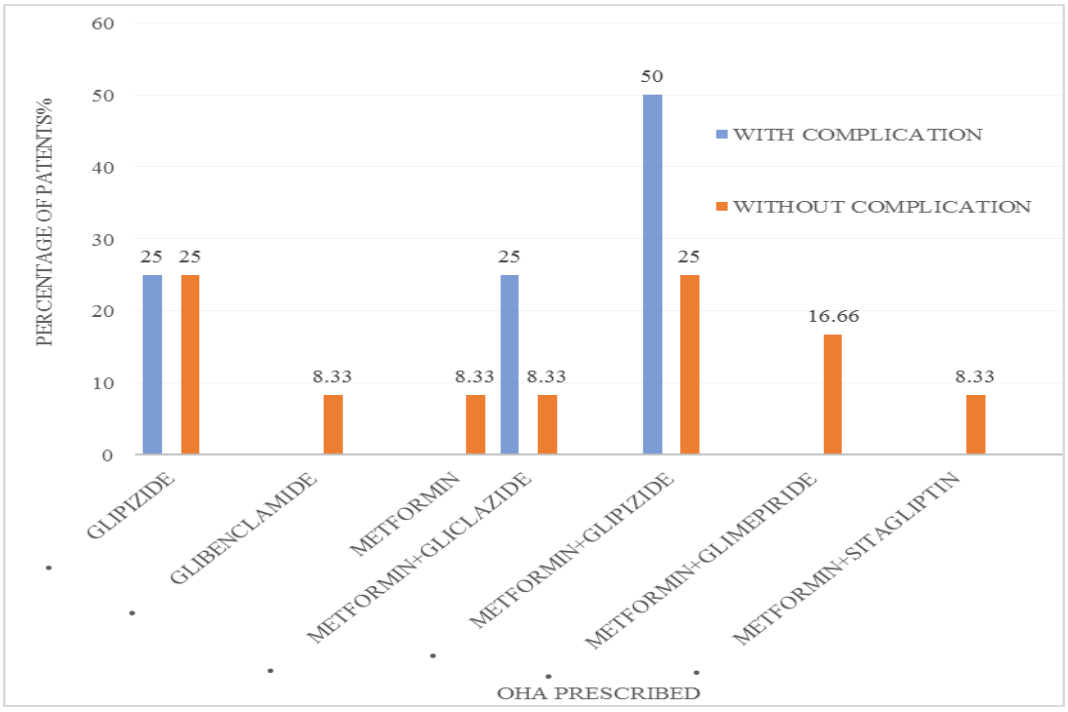

Figure 8: Distribution based on the hypoglycemia caused by oral hypoglycemic agents.

figure: 9 showed 2 distribution based on the hypoglycemia caused by OHA and insulin. In uncontrolled type 2 DM with complication (60%)hypoglycemia caused by 1 insulin and 2 OHA. Also, in uncontrolled type 2 DM without complication (66.66%) hypoglycemia caused by 1 insulin and 2 OHA .Similarly, in Varghese *et al.*1Insulin and 2 OHA leading to hypoglycemia. Because this prescribing pattern is common in type 2 diabetes mellitus.

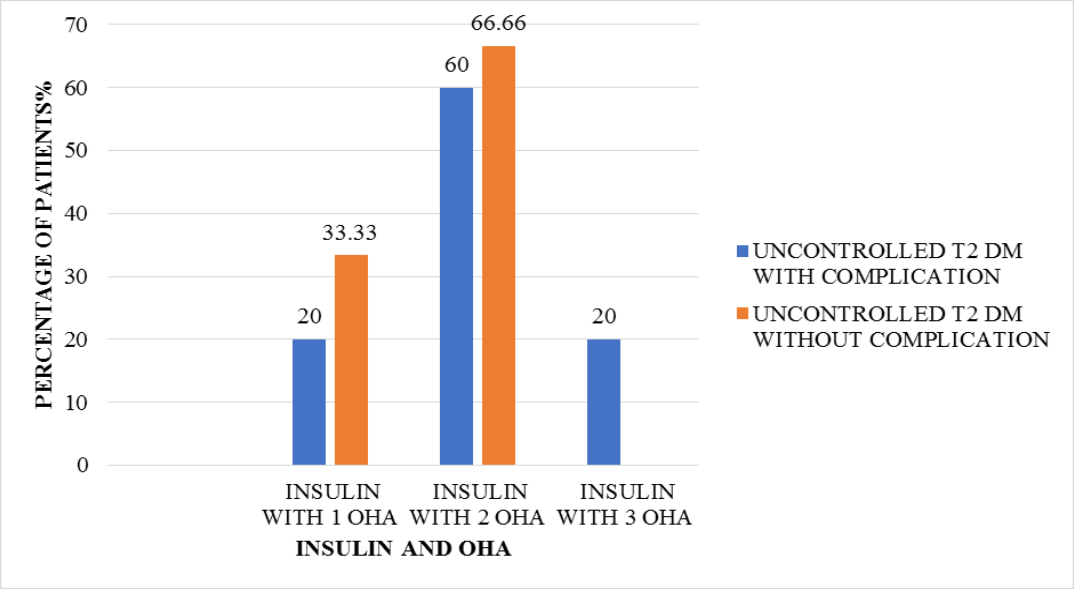

Figure 9: Distribution based on the hypoglycemia caused by oral hypoglycemic agents and insulin.

Table:6 showed distribution of ADR based on the Naranjo causality assessment scale. According to Naranjo causality assessment scale hypoglycemia more prone to definite type of ADR in both uncontrolled type 2 DM with complication (77.77%) and uncontrolled type 2 DM without complication (65.2%). In contrast to our study Singh A *et al*. according to Naranjo causality assessment scale probable and possible ADR were found to be most abundant with hypoglycemic events.[13]

Table 6: Distribution of ADR based on Naranjo causality assessment scale.

Naranjo Causality	Uncontrolled Type 2 DM With Complication		Uncontrolled Type 2 DM Without Complication	
	Number of Hypoglycemia (n=18)	Percentage (%)	Number of Hypoglycemia (n=23)	Percentage (%)
Definite (≥9)	14	77.77	15	65.21
Probable(5-8)	4	22.22	8	34.78
Possible (1-4)	0	0	0	0
Doubtful (≤0)	0	0	0	0

CONCLUSION

The study was aimed to assess the incidence, frequency and clinical manifestations of hypoglycemia. According to result, incidence of hypoglycemia more seen in uncontrolled type 2 DM with complication. Only one event of hypoglycemia seen in both uncontrolled type 2 DM with complication or without complication. Commonly multiple adrenergic signs or multiple neuroglycopenic or multiple adrenergic and neuroglycopenic symptoms were seen with hypoglycemia. In uncontrolled type 2 DM with complication both adrenergic signs and neuroglycopenic symptoms were mostly occurred. But in uncontrolled type 2 DM without complication multiple adrenergic signs are mostly occurred. In uncontrolled type 2 DM with complication hypoglycemic events are mainly caused by Insulin but in uncontrolled type 2 DM without complication combination of insulin and OHA caused hypoglycemia.

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