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Pharmacovigilance Study on Anti-diabetic Drugs

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Abstract

According to the World Health Organization (WHO), ADRs is defined as a response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of disease, or for the modification of physiological function. This definition excludes overdose, drug abuse, and treatment failure and drug administration errors. The female gender, age (very young and very old), multiple medications and the physiological state of renal and liver function, breastfeeding, pregnancy, and alcohol intake are considered as the important risk factors for ADR. The present study was carried out in Department of Diabetes, Govt. District Hospital, Dewas, (M.P), India. The data regarding Pharmacovigilance studies has been revealed in present communication.

Key words: Pharmacovigilance, Anti-diabetic, Drugs

Introduction

Diabetes mellitus (DM) is a syndrome with disordered metabolism and inappropriate hyperglycemia due to either a deficiency of insulin secretion or a combination of insulin resistance and inadequate insulin secretion. Pharmacovigilance is defined by the world health organization (WHO) as the science and activities relating to detection, assessment, understanding and prevention of adverse effects or any other drug-related problem.

ADRs are considered as one of the most important leading causes of mortality in many countries. ADR not only accounts for significant morbidity and mortality but can also lead to increase in the length of hospital stay and healthcare costs. The overall rate of ADRs is estimated to be 6.5%, and 28% of these ADRs are preventable as per WHO assessment. One of the meta-analysis found an ADR rate of 6.7% among hospitalized patients. The study of ADRs is the realm of what is known as pharmacovigilance. The WHO defines pharmacovigilance as "the science and activities relating to the detection, assessment, understanding, and prevention of ADRs or any other drug-related problems." It can help in providing continuous information on the safety of drug used. The increase in the prevalence of anti-diabetic medications highlights the need for the importance of clinical pharmacist for monitoring and reporting any suspected ADRs.

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To detect and analyze the ADRs in patients with diabetes mellitus with an assessment of causality, severity, and preventability in a Govt. hospital, the study has been carried out.

Methodology

Study area

The study was carried out in the Department of Diabetes, in Govt District Hospital, Dewas(M.P),India. It runs a separate diabetes department supported by a common ward, in-patient department (IPD).

Study period and study population

The study was conducted between 06/04/2017 to 07/05/2017. The patients admitted in the department of diabetes and treated with anti-diabetic drugs during the study period were included in the present study.

Study design

It was a hospital based prospective observational study. The patients were followed up for a period of 1month for observing adverse events after they had received the antidiabetic therapeutic drugs.

Inclusion and exclusion criteria

Among the patients receiving antidiabetic therapy, those who developed at least one Adverse drug reaction, were included in the study. The patients who did not show any ADR except urine discolouration were excluded from the study.

Study tools

Adverse drug reaction reporting form designed by Indian pharmacopoeia commission was used to collect the data regarding ADRs. One separate questionnaire regarding socio-demographic

characteristics was developed and used in the study. To assess the causality, WHO-UMC Causality AssessmentScale was used.

Statistical analysis

- After collection of data, it was entered in Microsoft Excel sheet. .One clean datasheet was generated and copied into prism software. Then the analysis was done in prism software.
- Identification of signals (i.e., possible causal relationships between an adverse event and a medicine) of ADRs of concern following the introduction of a new drug or drug combination.
- Assessment of signals to evaluate causality, clinical relevance, frequency and distribution of ADRs in particular population groups. Risk factors can be clearly identified by WHO-UMC causality assessment scales[45]; and severity assessment used hartwing scale,
- On behalf of scale, contribution to the assessment of benefit, harm, effectiveness and risk of medicines, leading to the prevention of harm and maximization of benefit; measurement and evaluation of the outcome of the response or of action taken e.g. reduction in risk, improved medicine use, or improved outcome for patients experiencing a particular ADR and provide feedback to the clinicians who provided the information.

WHO-UMC Causality Assessment Scale

Causality term	Assessment criteria
Certain	• Event of laboratory test abnormality, with plausible time relationship to drug intake • Cannot be explained by disease or other drugs • Response to withdrawal plausible (pharmacologically , pathologically) • Event definitive pharmacologically or phenomenological (i.e. an objective and specific medical disorder or a recognised pharmacological phenomenon) • Rechallenge satisfactory, if necessary
Probable/ Likely	• Event of laboratory test abnormality, with reasonable time relationship to drug intake • Unlikely to be attributed to disease or other drugs • Response to Withdrawal clinically reasonable • Rechallenge not required
Possible	• Event or laboratory test abnormality, with reasonable time relationship to drug intake • Could also be explained by disease or other drugs • Information on drug withdrawal may be lacking or unclear
Unlikely	• Event of laboratory test abnormality, with a time to drug intake that makes a relationship improbable (but not impossible) • Disease or other drugs provide plausible explanations
Conditional / Unclassified	• Event of laboratory test abnormality • More data for proper assessment needed, or • Additional data under examination
Unassessable / Unclassifiable	• Report suggesting an adverse reaction • Cannot be judged because information is insufficient or contradictory • Data cannot be supplemented or verified

Hartwig's Severity Assessment Scale

Level 1	An ADR occurred but required no change in treatment with the suspected drug.
Level 2	The ADR required that treatment with the suspected drug be held, discontinued, or otherwise changed. No antidote or other treatment requirement was required. No increase in length of stay (LOS).
Level 3	The ADR required that treatment with the suspected drug be held, discontinued, or otherwise changed. AND/OR An Antidote or other treatment was required. No increase in length of stay (LOS).
Level 4	Any level 3 ADR which increases length of stay by at least 1 day. OR the ADR was the reason for the admission.
Level 5	Any level 4 ADR which requires intensive medical care.
Level 6	The adverse reaction caused permanent harm to the patient.
Level 7	Adverse reaction either directly or indirectly led to the death of the patient.

Mild= level 1 and 2; Moderate= level 3 and 4; Severe= 5, 6 and 7.

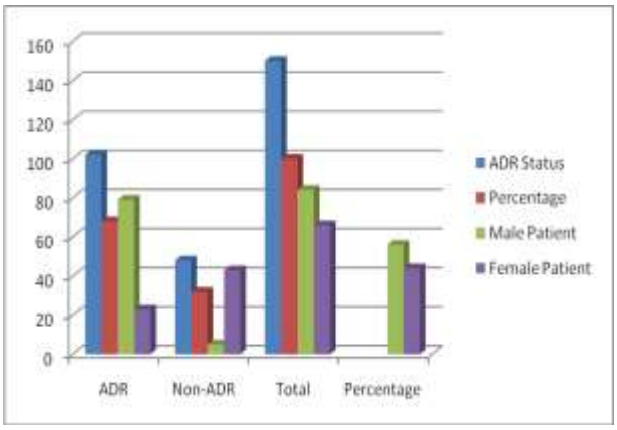
Results and Discussion

The present study was carried out in Department of Diabetes, Govt. District Hospital, Dewas, (M.P), India. It runs a separate diabetes department supported by a common ward and in-patient department (IPD). The study was conducted between 06/04/2017 to 07/05/2017 in the patients admitted in the Department of Diabetes and treated with anti-diabetic drugs during the study period were included in the present study and the follow up study was maintained for another 6 months for the complete analysis of data.

A total of 150 patient case sheets were reviewed (Table 1), 102 ADRs were reported from 79 male patient and 23 female patients during the study period. Incidence of ADRs occurrence was higher in male patients ([79] 77.45%) than female patients ([23] 22.54%). The data regarding the same was presented in Table 2:

Table 1: ADR characteristic's of study populations (n=150)

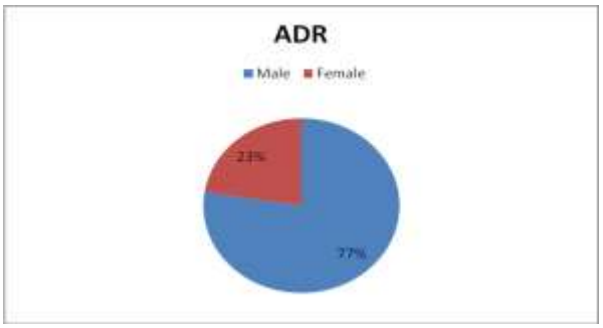
Characteristics	ADR	Non-ADR	Total	Percentage
ADR Status	102	48	150	-
Percentage	68	32	100	-
Male Patient	79	5	84	56
Female Patient	23	43	66	44



Graph 1: ADR characteristic's of study populations (n=150)

Table 2: Socio-demographic characteristics of study populations (n=102)

Characteristics	Male	Female
ADR	79	23
Percentage	77.45	22.54

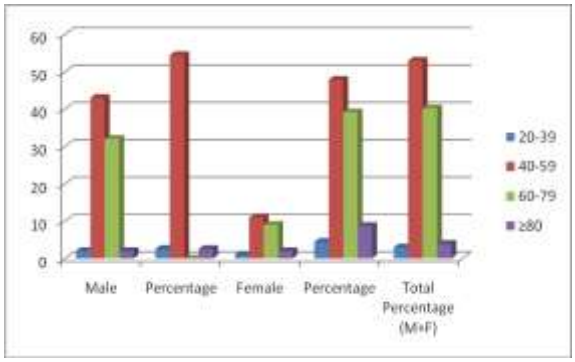


Graph 2: Socio-demographic characteristics of study populations (n=102)

The various age groups of the patients in the study were pointed out for both male and female patients. The results were presented in table 3. The results obtained indicate that the majority of the ADRs occurred in the age group of 40-59 years in case of male (43) & female (11) patient followed by age groups 60-79 years.

Table 3: Age wise distribution of ADR (n=102)

Age Groups	Male	Percentage	Female	Percentage	Total Percentage (M+F)
20-39	2	2.53	1	4.43	2.94
40-59	43	54.43	11	47.82	52.94
60-79	32	4-.50	9	39.13	40.19
≥80	2	2.53	2	8.69	3.92

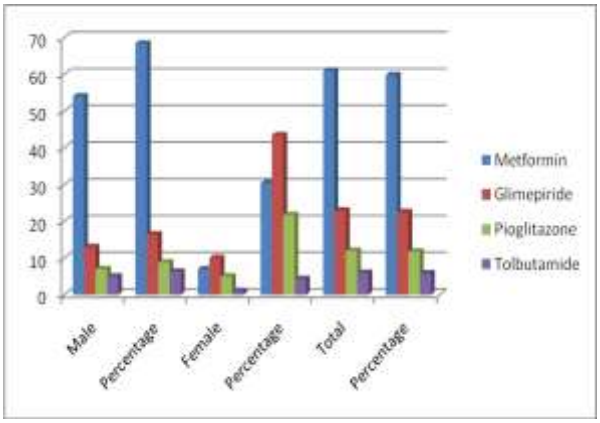


Graph 3: Age wise distribution of ADR (n=102)

The various drugs viz., Metformin, Glimepiride, Pioglitazone and Tolbutamide were prescribed to the 102 patients and the drug distribution were presented in table 4. Metformin was prescribed maximum to male patient (54) while Glimepiride as prescribed maximum to female patient (10).

Table 4: Distribution of Drug to patients (n=102)

Age Groups	Male	Percentage	Female	Percentage	Total	Percentage
Metformin	54	68.35	7	30.43	61	59.80
Glimepiride	13	16.45	10	43.47	23	22.54
Pioglitazone	7	8.86	5	21.73	12	11.76
Tolbutamide	5	6.32	1	4.34	6	5.88



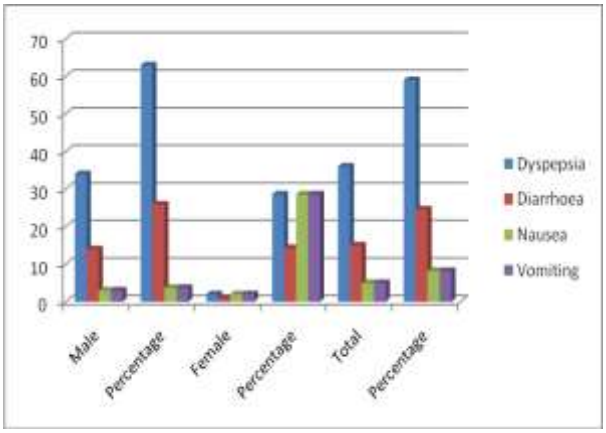
Graph 4: Distribution of Drug to patients (n=102)

The class of drugs most commonly responsible for causing ADRs was found to be Metformin (59.80%)

followed by Glimepride (22.54%), Pioglitazone (11.76%) and Tolbutamide (5.88%).

Table 5: ADR reports of Metformin (n=61; M=54; F=7)

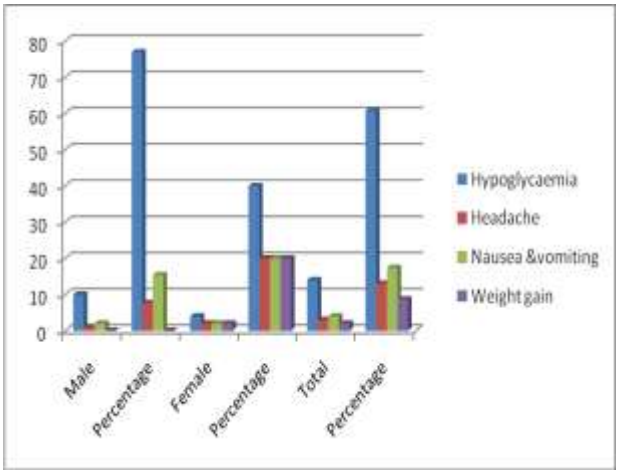
Age Groups	Male	Percentage	Female	Percentage	Total	Percentage
Dyspepsia	34	62.96	2	28.57	36	59.01
Diarrhoea	14	25.92	1	14.28	15	24.59
Nausea	3	3.70	2	28.57	5	8.19
Vomiting	3	3.70	2	28.57	5	8.19



Graph 5: ADR reports of Metformin (n=61; M=54; F=7)

Table 6: ADR reports of Glimepride (n=23; M=13; F=10)

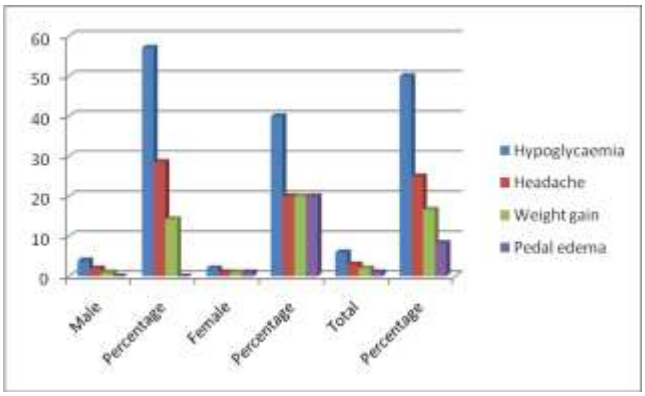
Age Groups	Male	Percentage	Female	Percentage	Total	Percentage
Hypoglycaemia	10	76.92	4	40.0	14	60.86
Headache	1	7.69	2	20.0	3	13.04
Nausea &vomiting	2	15.38	2	20.0	4	17.39
Weight gain	0	0	2	20.0	2	8.69



Graph 6: ADR reports of Glimepride (n=23; M=13; F=10)

Table 7: ADR reports of Pioglitazone (n=12; M=7; F=5)

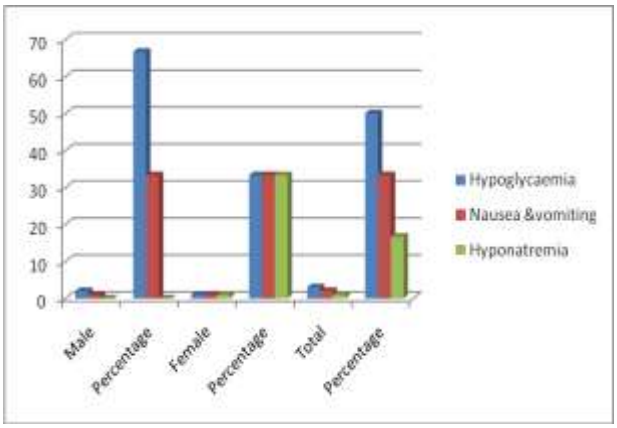
Age Groups	Male	Percentage	Female	Percentage	Total	Percentage
Hypoglycaemia	4	57.14	2	40.0	6	50.0
Headache	2	28.57	1	20.0	3	25.0
Weight gain	1	14.28	1	20.0	2	16.66
Pedal edema	0	0	1	20.0	1	8.33



Graph 7: ADR reports of Pioglitazone (n=12; M=7; F=5)

Table 8: ADR reports of Tolbutamide (n=6; M=3; F=3)

Age Groups	Male	Percentage	Female	Percentage	Total	Percentage
Hypoglycaemia	2	66.66	1	33.33	3	50.0
Nausea &vomiting	1	33.33	1	33.33	2	33.33
Hyponatremia	0	0	1	33.33	1	16.66

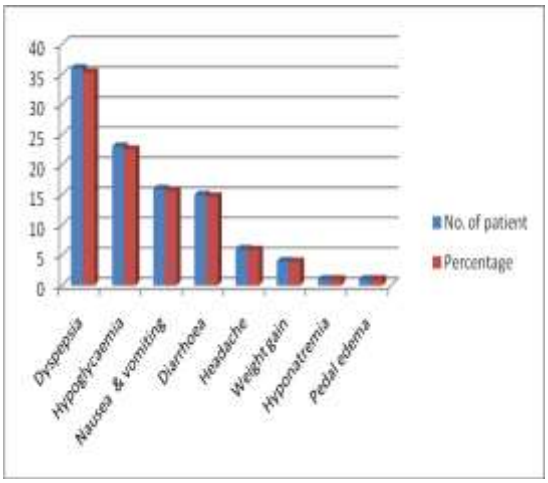


Graph 8: ADR reports of Tolbutamide (n=6; M=3; F=3)

The most commonly occurred ADRs was dyspepsia (35.29%) followed by hypoglycemia (22.51%), nausea & vomiting (15.68%), diarrhea (14.74%), headache (5.88%), weight gain (3.92%), hyponatremia (0.98%) and pedal edema (0.98%)

Table 9: ADR reports of prescribed anti-diabetic drug (n=102)

Adverse effects	No. of patient	Percentage
Dyspepsia	36	35.29
Hypoglycaemia	23	22.51
Nausea & vomiting	16	15.68
Diarrhoea	15	14.74
Headache	6	5.88
Weight gain	4	3.92
Hyponatremia	1	0.98
Pedal edema	1	0.98

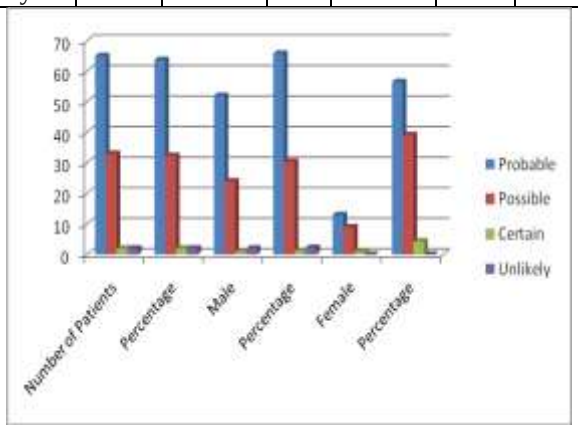


Graph 9: ADR reports of prescribed anti-diabetic drug (n=102)

The suspected ADRs were assessed for their causality using the Naranjo algorithm probability scale. It was revealed that 59.80% were probable, 37.25% were possible, and 2.94% were definite. The results were presented in table 10.

Table 10: Causality assessment among patient shows ADR (n=102; M=79; F=23))

Causality Assessment	Number of Patients	Percentage	Male	Percentage	Female	Percentage
Probable	65	63.72	52	65.822	13	56.52
Possible	33	32.35	24	30.37	9	39.13
Certain	2	1.96	1	1.26	1	4.34
Unlikely	2	1.96	2	2.25	0	0

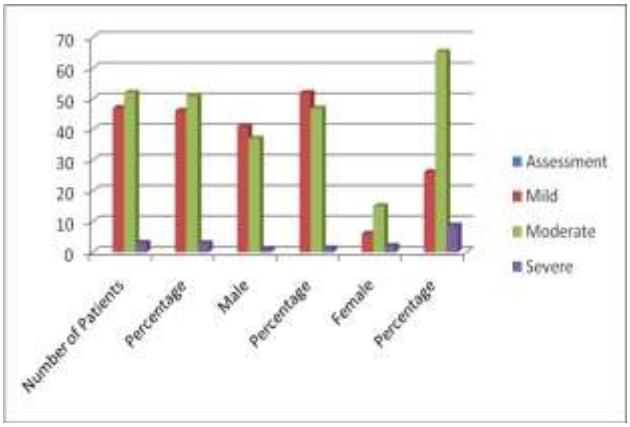


Graph 10: Causality assessment among patient shows ADR (n=102; M=79; F=23))

The ADRs were assessed for their severity using a modified Hartwig severity scale, which is a standard scale for severity assessment. It was observed that 46.06 % were mild, 50.98 % were moderate, and 2.94 % were severe. The results were presented in table 11.

Table 11: ADR assessment among patient using Hartwig severity scale (n=102; M=79; F=23))

Severity Assessment	Number of Patients	Percentage	Male	Percentage	Female	Percentage
Mild	47	46.06	41	51.89	6	26.08
Moderate	52	50.98	37	46.83	15	65.21
Severe	3	2.94	1	1.26	2	8.69

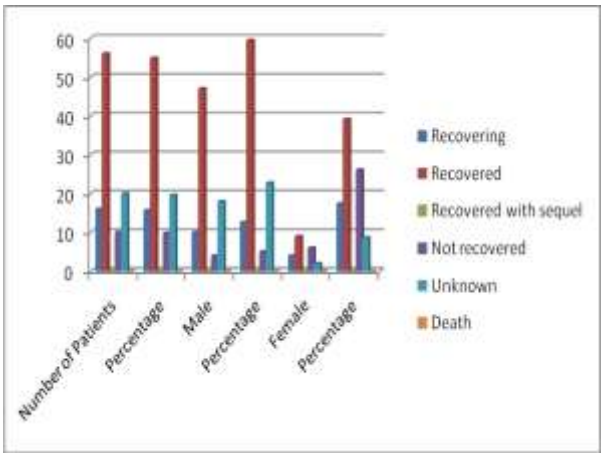


Graph 11: ADR assessment among patient using Hartwig severity scale (n=102; M=79; F=23))

Preventability of the reported ADRs was assessed using the "modified Schumock and Thornton preventability scale." Using this scale, results revealed that 56 (54.90%) were recovered while 16(15.68%) were recovering. Tee detailed results were presented in table 12.

Table12: ADR assessment among patient using Hartwig severity scale (n=102; M=79; F=23))

Dechallenge/ outcome	Number of Patients	Percentage	Male	Percentage	Female	Percentage
Recovering	16	15.68	10	12.65	4	17.39
Recovered	56	54.90	47	59.49	9	39.13
Recovered with sequel	0	0	0	0	0	0
Not recovered	10	9.80	4	5.06	6	26.08
Unknown	20	19.60	18	22.78	2	8.69
Death	0	0	0	0	0	0



Graph 12: ADR assessment among patient using Hartwig severity scale (n=102; M=79; F=23))

References

1. BhattacharjeeA, Gupta MC,and Agrawal S (2016).Adverse drug reaction monitoring of newer oral anti-diabetic drugs – A pharmacovigilance perspective, *International Journal of Pharmacological Research* , 6(4):142.
2. Longo DL, Kasper DL, Jameson JL, Fauci AS, Hauser SL, Loscalzo J, and Harrison's, (2012). Principle of internal medicine, *New York: Mcgraw Hill:*18:2968-3002.
3. http://www.diabetes.co.uk (2016). The global diabetes community.
4. Mane P, Antre RV, andOswal RJ (2012).Antidiabetic drugs: An overview,*International Journal of Pharmaceutical and Chemical Sciences*, 1(1):304-305.
5. Tripathi KD (2014).Essentials of medical pharmacoloy,*Jaypee Brothers Medical Publishers (P) Ltd*, 7(7):270-271.

6. http://www.world health organization (2016). Global report on diabetes
7. National institute of diabetes and digestive and kidney diseases (2016).
8. International diabetes federation (2015).
9. Diabetes Australia (2015). Or https://www.diabetesaustralia.com.au
10. Ozaugwu, JC, Obimba KC, Belonwu CD, Unakalamba CB (2013).The pathogenesis and pathophysiology of type 1 and type 2 diabetes mellitus, *Journal of Physiology and Pathophysiology* , 4(4):46-57.
11. WHO (2006). Definitionand diagnosis of diabetes mellitus and intermediate hyperglycemia.
12. Gelaw BK (2014).Non adherence and contributing factors among ambulatory patients with anti-diabetic medications in adama referral hospital,*Advances in Pharmacoepidemiology and Drug Safety*, 3[4]:2.
13. Barrett-Connor E, and Ferrara A(1998). Isolated postchallenge hyperglycemia and the risk of fatal cardiovascular disease in older women and men: the Rancho Bernardo Study. Diabetes Care, 21:1236–1239.
14. DECODE study group (2001). Glucose tolerance and cardiovascular mortality. Comparison of fasting and 2-hour diagnostic criteria. *Arch Int Med*, 161:397-404.
15. Shaw JE, Hodge AM, de Courten M, Chitson P, andZimmet PZ(1999). Isolated post-challenge hyperglycaemia confirmed as a risk factor for mortality. Diabetologia, 42:1050–1054.

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