

# Assessment of the Level of Adherence to Insulin Therapy and Diet Recommendations Among Diabetes Patient

Ola Abd Al-Latif Hamid<sup>1\*</sup>, Ameer Kadhim Al-Humairi<sup>2</sup>

<sup>1</sup> College of Medicine, University of Babylon, Babylon, Iraq.

<sup>2</sup>Community Medicine, College of Medicine, University of Babylon, Babylon, Iraq.

Received: 19th September, 2020; Revised: 16th October, 2020; Accepted: 04th November, 2020; Available Online: 25th March, 2021

## ABSTRACT

**Background:** Diabetes mellitus is a common chronic metabolic disorder characterized by hyperglycemia and disturbances in metabolism, with rising prevalence globally due to various factors such as aging, decreased physical activity and increasing obesity. Optimal adherence of diabetic patients both with insulin treatment and dietary recommendations is necessary to achieve the full clinical benefit of therapy.

**Objectives of the Study:** Assessment of adherence to insulin therapy and adherence to diet restriction among diabetic patients.

**Methodology:** Cross-sectional study conducted in Merjan Teaching Hospital, Al-Hilla Teaching Hospital, Al-Hussein Teaching Hospital, and Diabetes Disease Center in Babylon and Thi-Qar governorates, and included 151 diabetic patients during the period from February-June 2020. Data were collected using a specially designed questionnaire form that includes the standardized Morisky Medication Adherence Scale-8 (MMAS-8) to assess insulin therapy adherence and diet restriction.

**Results:** Males formed 50.3% of the study sample. Majority (44.4%) were overweight (BMI 25–29.9). Only 23.8% of patients had high adherence to insulin therapy, while 49.0% had low adherence. Insulin adherence was significantly correlated with RBS, HbA1c, occupation, and SES ( $p < 0.05$ ). Adherence to diet was significantly associated with RBS, HbA1c, adherence to insulin, gender, marital status, and occupation ( $p < 0.05$ ).

**Conclusions:** Adherence to insulin therapy was low in almost half of patients. It was found that the level of adherence significantly impacted glycemic control. Adherence to dietary recommendations was closely correlated with insulin adherence.

**Keywords:** Adherence, Diabetes, Dietary recommendations, Insulin.

International Journal of Drug Delivery Technology (2021); DOI: 10.25258/ijddt.11.1.38

**How to cite this article:** Al-Latif Hamid OA, Al-Humairi AK. Assessment of the Level of Adherence to Insulin Therapy and Diet Recommendations Among Diabetes Patient. International Journal of Drug Delivery Technology. 2021;11(1):204-208.

**Source of support:** Nil.

**Conflict of interest:** None

## INTRODUCTION

Diabetes mellitus (DM) refers to a common chronic metabolic disorder characterized by both chronic hyperglycemia and disturbances in the metabolism of carbohydrates, proteins, and fats.<sup>1</sup> Its prevalence is rising globally, causing a significant public health burden globally.<sup>2</sup> Various factors contribute to this sustained increase in prevalence, including aging, decreased physical activity and increasing obesity.<sup>3</sup> The prevalence rate of diabetes among the Iraqi population is 143.8 per 1000 persons in people aged 50 years or older, as estimated by IFHS 2006/7: a national survey conducted during 2006-2007 in Iraq.<sup>4</sup>

Diabetes mellitus (DM) is classified into three main types: Type 1 (insulin-dependent), type 2 (non-insulin-dependent), and gestational diabetes. It is diagnosed using plasma glucose level and glycated hemoglobin proportion.<sup>1,5</sup> Symptoms of type 1 diabetes mellitus are more severe than those of type 2

diabetes (T2D); they generally include thirst, polyurea, lack of energy, polyphagia, recurrent infections, the rapid loss of weight, and blurring of vision.<sup>6</sup>

Various complications are associated with diabetes mellitus, some are acute in onset such as ketoacidosis and severe hyperglycemia, which can be life-threatening; while others are long-term debilitating complications, such as nephropathy, retinopathy, neuropathy, as well as complications of the cardiovascular system.<sup>7</sup> Diabetes mellitus also increases the susceptibility to infections.<sup>8</sup> Management of diabetes mainly depends on the disease type.<sup>1,5</sup>

Adherence is defined as, the extent to which a person's behavior in taking medication, following a diet, and/or executing lifestyle changes corresponds with agreed recommendations from a healthcare provider.<sup>9</sup> Optimal adherence of diabetic patients with insulin treatment and dietary recommendations is necessary to achieve the treatment

\*Author for Correspondence: aualaabdullatif@gmail.com

regimen's full clinical benefit.<sup>10,11</sup> However, certain barriers exist that can substantially restrict and limit the patients' adherence, therefore impacting the effectiveness of the regimen.<sup>12</sup>

Dietary recommendations regarding diabetes patients aim to maintain healthy weight with balanced energy intake,

promote the pattern of food intake, and reduce consumption of refined sugars and grains and processed red meats.<sup>14,15</sup>

**Objective of the Study**

To assess the adherence to insulin therapy and to diet restriction among diabetic patients.

**Table 1:** Distribution of patients according to study characteristics (N = 151)

<i>Socio-demographic characteristics</i>		
<i>Age (years)</i>	<i>(47.25 ± 18.95)</i>	<i>(8–85)</i>
<i>Gender</i>		
Male	76	50.3%
Female	75	49.7%
<i>Residence</i>		
Urban	90	59.6%
Rural	61	40.4%
<i>Marital status</i>		
Married	104	68.9%
Single	36	23.8%
Divorced	3	2.0%
Widow	8	5.3%
<i>Educational level</i>		
Illiterate	31	20.5%
Primary	48	31.8%
Secondary	38	25.2%
Higher education	34	22.5%
<i>Occupation</i>		
Employee	36	23.8%
free worker	39	25.8%
Housewife	41	27.2%
Student	22	14.6%
Retired	13	8.6%
<i>Socio-economic status</i>		
< 500000 Iraqi Dinar/ month	66	43.7%
500000-1000000 Iraqi Dinar/ month	60	39.7%
>1000000 Iraqi Dinar/ month	25	16.6%
<i>Smoking habit (cigarette)</i>		
Current Smoker	38	25.2%
Non-smoker	95	62.9%
Ex- smoker	18	11.9%
Total	151	100.0%

**PATIENTS AND METHODS**

This is a cross-sectional study conducted at Merjan Teaching Hospital, Al-Hilla Teaching Hospital, Al-Hussein Teaching Hospital, and Diabetes Disease Center in Babylon and Thi-Qar governorates to assess the adherence to insulin therapy and diet recommendation among diabetic patients for 5 months from February to June 2020. And included patients with type 1 and type 2 diabetes who are taking insulin therapy and who were accepted to participate in the study during a period of data collection. According to the Fisher formula, the sample size was calculated to be 150 patients with type 1 and type 2 DM who visited the four mentioned hospitals.

Data were collected using a specially designed questionnaire that includes socio-demographic characteristics, details about diabetes including duration of disease, type and duration of insulin therapy, biochemical investigations, as well as any chronic diseases. Standardized score was used to assess the adherence to insulin therapy which comprised the second part of the questionnaire, this score is called “Morisky Medication Adherence Scale-8” (MMAS-8), which contains 8-item scale. Items (1–7) have response choices yes or no whereas item 8 has 5-point response choices. Each no response is rated as 1 and each yes is rated as 0 except for item 5, in which each yes answer is rated as 1 and each no answer is rated as 0. For item 8, if a patient chooses response 4, the score will be 1, and if they choose a response 0 the score is zero. Responses 1, 2, and 3 are respectively rated as 0.25, 0.75, and 0.75. Total MMAS-8 scores can range from 0 to 8 and have been classified into three levels of adherence: high adherence (score = 8), medium adherence (score = 6-< 8), and low adherence (score <6).<sup>16-19</sup>

Diet recommendations score consisted the third part of the questionnaire, which include twenty questions. The

**Table 2:** The mean differences of study variables according to adherence to insulin therapy.

<i>Study variables</i>	<i>Adherence to insulin therapy</i>	<i>N</i>	<i>Mean</i>	<i>SD</i>	<i>F-test</i>	<i>p-value</i>
Age (years)	Low (score < 6)	74	49.61	19.48	1.212	0.301
	Medium (score 6 -<8)	41	44.15	21.76		
	High (score 8)	36	45.94	13.44		
BMI (kg/m2)	Low (score < 6)	74	27.33	4.25	0.891	0.412
	Medium (score 6 -<8)	41	26.40	2.94		
	High (score 8)	36	27.22	3.22		
RBS (mg/dl)	Low (score < 6)	74	312.72	107.87	29.15	<0.001*
	Medium (score 6 -<8)	41	233.46	88.57		
	High (score 8)	36	172.47	60.97		
HBA1C (%)	Low (score < 6)	74	8.67	1.480	17.60	<0.001*
	Medium (score 6 -<8)	41	7.80	1.44		
	High (score 8)	36	7.09	0.85		

\*p-value ≤0.05 was significant.

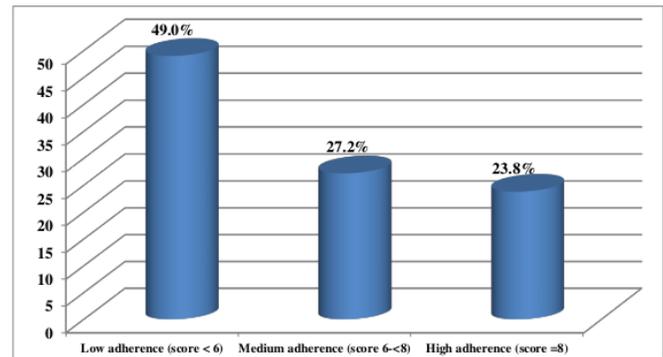
result of this score was calculated by giving one degree for right answer and zero for the wrong answer.<sup>20</sup> Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) version 25 (IBM Company, Chicago, USA).

**RESULTS AND DISCUSSION**

This cross-sectional study included a total of 151 diabetic patients, whose age ranged from 8 to 85 years, with a mean age of (47.25 ± 18.95) years, with almost equal proportions of male and female patients. This age was slightly younger than the age reported by Al-Dalawi and Al-Humairi in their study conducted in Merjan hospital and Al-Hilla teaching hospital in 2019, who reported age of 54.96 ± 12.51 years.<sup>21</sup>

Regarding the residence of study participants, higher proportion (59.6%) were from urban areas while the remaining 40.4% were from rural areas. This is similar to the finding reported by Al-Dalawi and Al-Humairi, who also reported a

higher proportion from urban areas.<sup>21</sup> Married participants constituted the majority of study sample (68.9%), which was slightly higher than the proportion of married participants



**Figure 1:** Distribution of patients according to adherence to insulin therapy

\*Mean score was 5.25 ± 2.57.

**Table 3:** Association between adherence to insulin therapy and socio-demographic characteristics

Study variables	Adherence to insulin therapy			χ <sup>2</sup>	p-value
	Low (<6)	Medium (6-<8)	High (8)		
<i>Gender</i>					
Male	41 (55.4)	16 (39.0)	19 (52.8)	2.94	0.229
Female	33 (44.6)	25 (61.0)	17 (47.2)		
Total	74 (100.0)	41 (100.0)	36 (100.0)		
<i>Residence</i>					
Rural	35 (47.3)	15 (36.6)	11 (30.6)	3.15	0.206
Urban	39 (52.7)	26 (63.4)	25 (69.4)		
Total	74 (100.0)	41 (100.0)	36 (100.0)		
<i>Educational level</i>					
Illiterate	19 (25.7)	7 (17.1)	5 (13.9)	5.18	0.52
Primary	21 (28.4)	17 (41.5)	10 (27.8)		
Secondary	19 (25.7)	8 (19.5)	11 (30.5)		
Higher education	15 (20.3)	9 (22.0)	10 (27.8)		
Total	74 (100.0)	41 (100.0)	36 (100.0)		
<i>Marital status</i>					
Married	51 (68.9)	26 (63.4)	27 (75.0)	0.535 f	
Single	18 (24.3)	12 (29.3)	6 (16.7)		
Divorce	1 (1.4)	0 (0.0)	2 (5.6)		
Widow	4 (5.4)	3 (7.3)	1 (2.8)		
Total	74 (100.0)	41 (100.0)	36 (100.0)		
<i>Occupation</i>					
Employee	11 (14.9)	9 (22.0)	16 (44.4)	22.93	0.003*
Free work	25 (33.8)	6 (14.6)	8 (22.2)		
Housewife	21 (28.4)	10 (24.4)	10 (27.8)		
Student	10 (13.5)	11 (26.8)	1 (2.8)		
Retired	7 (9.5)	5 (12.2)	1 (2.8)		
Total	74 (100.0)	41 (100.0)	36 (100.0)		
<i>Socio-economic status</i>					
<500000 Iraqi dinar	36 (48.6)	19 (46.3)	11 (30.6)	15.09	0.005*
500000-1000000 Iraqi dinar	34 (45.9)	12 (29.3)	14 (38.8)		
>1000000 Iraqi dinar	4 (5.4)	10 (24.4)	11 (30.6)		
Total	74 (100.0)	41 (100.0)	36 (100.0)		
<i>Smoking habit</i>					
Smoker	18 (24.3)	10 (24.4)	10 (27.8)	0.943 f	
None smoker	47 (63.5)	25 (61.0)	23 (63.9)		
Ex-smoker	9 (12.2)	6 (14.6)	3 (8.2)		
Total	74 (100.0)	41 (100.0)	36 (100.0)		

\*p value ≤0.05 was significant.

**Table 4:** The correlation between study variables and adherence to diet recommendation.

Study variables	N	Mean	SD	r	p-value
adherence to diet recommendation score	151	13.35	2.91		
Age	151	47.25	18.95	0.119	0.147
adherence to diet recommendation score	151	13.35	2.91		
BMI (kg/m <sup>2</sup> )	151	27.05	3.70	-0.003	0.969
adherence to diet recommendation score	151	13.35	2.91		
RBS (mg/dl)	151	257.76	109.63	-0.548	<0.001*
adherence to diet recommendation score	151	13.35	2.91		
HBA1C (%)	151	8.05	1.49	-0.427	<0.001*
adherence to diet recommendation score	151	13.35	2.91		
adherence to insulin score	151	5.25	2.57	0.336	<0.001*

reported in the study by Mariye *et al.* in their study conducted in 2018, which included a total of 273 participants.<sup>23</sup>

About one-fifth of the study sample, 20.5% were illiterate regarding the educational level of participants. This is closely similar to the finding of 20.0% reported by Al-Dalawi and Al-Humairi in their study.<sup>21</sup> However, this proportion was lower than the proportion of 37.34% reported by Alsayed and Ghoraba in their study conducted in Saudi Arabia in 2018.<sup>22</sup> Regarding occupation, almost similar proportions were employees, free workers, and housewives, constituting about one-quarter each. Smokers formed 25.2% of study participants, while non-smokers formed 62.9% of them. These proportions are in agreement with the study by Al-Dalawi and Al-Humairi.<sup>21</sup>

The majority of patients within the study samples had a body-mass index (BMI) between 25.0–29.9 kg/m<sup>2</sup>. This finding clearly elucidate the relationship between increased BMI and the prevalence of diabetes mellitus, which is consistent with the findings reported by Alhazmi *et al.* in 2017.<sup>24</sup>

Low medication adherence (Morisky Medication Adherence score <6) was observed in almost half of the patients 49.0%. This was slightly lower than that reported by Al-Haj Mohd *et al.* conducted in the United Arab Emirates, who reported that 64.6% of their patients had less than six adherence scores.<sup>25</sup> However, Farsaei *et al.* conducted a study in Iran in 2014 found a proportion of 21.65% with low medication adherence.<sup>26</sup> In contrast, the study by Jarab *et al.* conducted in Jordan in 2014 had demonstrated that 72.5% of the patients had poor adherence.<sup>27</sup>

In addition, medium adherence (score 6-<8) and high adherence (score = 8) were observed in (27.2%) and (23.8%), respectively, giving a total of (51.0%) with medium-to-high adherence. The medium adherence proportion was closely similar to that reported by Al-Haj Mohd *et al.* (26.5%), but the high adherence proportion in the present study was markedly higher than the proportion of (9.0%) reported by Al-Haj Mohd (Al-Haj Mohd *et al.*, 2016). In Jordan, the study by Jarab *et al.* in Jordan had demonstrated that the proportion of patients with medium-to-high adherence was 27.5%,<sup>27</sup> which was markedly lower than the finding of this study (51.0%). These variations could be attributed to the variation in dietary habits of different populations.

Adherence to insulin therapy was compared with the various study variables. There was no significant relationship between age and adherence to insulin therapy (p-value = 0.301). This finding was similar to the finding by Nonogaki *et al.* in their study. They similarly reported that no significant relationship was observed between adherence and age, with p-value of 0.241.<sup>28</sup> Similarly, there was no significant relationship between BMI and adherence level in the present study, with p-value of 0.412. The finding supported this finding by Osborn and Gonzalez in their study conducted in the United States of America.<sup>29</sup>

No gender difference regarding adherence to insulin therapy was observed in the present study (p-value = 0.229). This finding is consistent with the finding reported by Osborn and Gonzalez.<sup>29</sup> A similar finding was presented by Jarab *et al.*, who described no significant relationship between level of adherence and gender, with p-value of 0.693.<sup>27</sup>

A residence was also found to have no significant relationship with level of adherence (P-value = 0.206). This was consistent with the finding reported by Aladhab and Alabbod in their study conducted in Basra governorate in 2018 (Aladhab R and Alabbod M, 2019). Similarly, level of education was also not significantly correlated with level of adherence, which was also similar to the finding by Aladhab and Alabbod.<sup>30</sup>

Both occupation and monthly income were found to be significantly correlated with the level of adherence to insulin therapy, with a p-value of 0.003 and 0.005, respectively. A study by Houle *et al.* had thoroughly examined the relationship between socioeconomic status and glycemic control and suggested that the implication of socioeconomic status on the glycemic control is attributed to several characteristics, these include the perception of patients of their disease, the way they cope with illness-related stress, the composition of their diets, as well as psychological status; especially depressive symptoms.<sup>31</sup>

No correlation was observed between insulin therapy adherence and any smoking habit, history of chronic diseases, duration of diabetes, or type of treatment (whether it includes hypoglycemic agents or not), with p-values of 0.943, 0.400, 0.301, and 0.298, respectively.

There was a strong negative correlation between adherence to dietary recommendations and each of RBS level and HbA1c

level regarding adherence to dietary recommendations. This clearly reflects the necessary role of following dietary recommendations in order to achieve proper glycemic control.

A study similar to the present study demonstrated that non-adherence to dietary recommendations by diabetic patients is associated with higher levels of blood glucose and cholesterol and eventually leads to complications.<sup>32</sup>

## REFERENCES

- World Health Organization. Use of Glycated Haemoglobin (HbA1c) in the Diagnosis of Diabetes Mellitus. *Abbreviated report of a WHO consultation*, WHO/NMH/CHP/CPM/11.1, 2011.
- Wild S, Roglic G, Green A, Sicree R, King H. Global Prevalence of Diabetes: Estimates for the year 2000 and projections for 2030. *Diabetes Care*. 2004;27(5):1047-1053.
- Cho H. The Association between Serum GGT Concentration and Diabetic Peripheral Polyneuropathy in Type 2 Diabetic Patients. *Korean Diabetes Journal*. 2010;34(2):111-118.
- MoH Iraq. Iraq Family Health Survey 2006/7: Prevalence of non communicable diseases and risk factors in Iraq, A step wise approach. National survey implemented by Ministry of Health, Directorate of Public Health and Primary Health Care and Ministry of Planning and Development Cooperation in collaboration with World Health Organization (WHO)/Iraq-Baghdad, 2006/7.
- Otto-Buczowska E, Jainta N. Pharmacological Treatment in Diabetes Mellitus Type 1 – Insulin and What Else? *Endocrinology & Metabolism International Journal*. 2018 ;16(1):e13008.
- Kharroubi A, Darwish H. Diabetes mellitus: The epidemic of the century. *World Journal of Diabetes*. 2015;6(6):850-867.
- Nickerson H, Dutta S. Diabetic Complications: Current Challenges and Opportunities. *Journal of Cardiovascular Translational Research*. 2012;5:375-379.
- Jafar N, Edriss H, Nugent K. The Effect of Short-Term Hyperglycemia on the Innate Immune System. *The American Journal of The Medical Sciences*. 2016;351(2):201-211.
- Azevedo M, Alla S. Diabetes in sub-saharan Africa: Kenya, Mali, Mozambique, Nigeria, South Africa and Zambia. *International Journal of Diabetes in Developing Countries*. 2008;28(4):101-108.
- He X, Chen L, Wang K, Wu H, Wu J. Insulin adherence and persistence among Chinese patients with type 2 diabetes: a retrospective database analysis. *Patient Preference and Adherence*. 2017;11:237-245.
- Jaworski M, Panczyk M, Cedro M, Kucharska A. Adherence to dietary recommendations in diabetes mellitus: disease acceptance as a potential mediator. *Patient Preference and Adherence*. 2018;12:163-174.
- American Diabetes Association. Standards of Medical Care in Diabetes – 2016 Abridged for Primary Care Providers. *Clinical Diabetes*. 2016;34(1):3-21.
- Forouhi N, Misram A, Mohan V, Taylor R, Yance W. Dietary and nutritional approaches for prevention and management of type 2 diabetes. *BMJ*. 2018;361:1-9.
- American Diabetes Association. Lifestyle Management: Standards of Medical Care in Diabetes – 2019. *Diabetes Care*. 2019;42(1):S46-S60.
- Charan J, Biswas T. How to calculate sample size for different study designs in medical research. *Indian Journal of Psychological Medicine*. 2013;35(2):121-126.
- Morisky D, Green L, Levine D. Concurrent and predictive validity of a self-reported measure of medication adherence. *Medical Care*. 1986;24(1):67-74.
- Vasam P, Kommoju HL, Govathoti D, Kolanedi AP, Krishna G, Reddy L. A Study on Assessment of Medication Adherence And Its Factors Among Elderly Patients in-out Patient Department in Tertiary Care Hospital. *Int Res J Pharm*. 2015;6(9):649-55.
- Samson Okello, Benson Nasasira, Anthony NdichuWamuiru, Anthony Musingo. Validity and Reliability of a Self-Reported Measure of Antihypertensive Medication Adherence in Uganda. *PLOS ONE* | DOI:10.1371/journal.pone.0158499 July 1, 2016. P:1-11.
- Anju P R, Abubaker Siddiq. A Study of Medication Adherence and Medication Compliance to Insulin Therapy in Type I and Type II, Diabetic Patients. *Indian Journal of Pharmacy Practice*, Vol 11, Issue 3, 2018. P:130-133.
- Mariusz Jaworski, Mariusz Panczyk, Małgorzata Cedro, Alicja Kucharska. Adherence to dietary recommendations in diabetes mellitus: disease acceptance as a potential mediator. *Patient Preference and Adherence* 2018;12 163–174
- Al-Dalawi A, Al-Humairi A. Assessment Of Awareness About Foot Care Among Diabetic Patients With or Without Foot Ulcer. *Annals of Tropical Medicine & Public Health*, 2019;22(10):S290.
- Alsayed Kh, Ghoraba M. Assessment of diabetic patients' adherence to insulin injections on basal-bolus regimen in diabetic care center in Saudi Arabia 2018: Cross sectional survey. *Journal of Family Medicine and Primary Care*. 2019;8:1964-1970.
- Mariye T, Girmay A, Birhanu T et al. Adherence to insulin therapy and associated factors among patients with diabetes mellitus in public hospitals of Central Zone of Tigray, Ethiopia, 2018: a cross-sectional study. *Pan African Medical Journal*. 2019;33(309):1-10.
- Alhazmi R., Ahmed A, Alshalan M et al. Prevalence of diabetes mellitus and its relation with obesity in Turaif (Saudi Arabia) in 2017. *Electron Physician*. 2017;9(10):5531-5535.
- Al-Haj Mohd M, Phung H, Sun J, Morisky D. Improving adherence to medication in adults with diabetes in the United Arab Emirates. *BMC Public Health*. 2016;16(857):1-10.
- Farsaei S, Radfar M, Heydari Z et al. Insulin adherence in patients with diabetes: Risk factors for injection omission. *Primary Care Diabetes*. 2014;8(4):338–345.
- Jarab A, Almrayat R, Alqudah S et al. Predictors of non-adherence to pharmacotherapy in patients with type 2 diabetes. *International Journal of Clinical Pharmacy*. 2014;36(4):725–733.
- Nonogaki A, Heang H, Yi S et al. Factors associated with medication adherence among people with diabetes mellitus in poor urban areas of Cambodia: A cross-sectional study. *PLOS ONE*. 2019;14(11):1-17.
- Osborn Ch, Gonzalez J. Measuring Insulin Adherence among Adults with Type 2 Diabetes. *Journal of Behavioral Medicine*. 2016;39(4):633-641.
- Aladhab R, Alabbod M. Adherence of Patients with Diabetes to a Lifestyle Advice and Management Plan in Basra, Southern Iraq. *International Journal of Diabetes and Metabolism*. 2019:1-5.
- Houle J, Lauzier-Jobin F, Beaulieu M et al. Socioeconomic status and glycemic control in adult patients with type 2 diabetes: a mediation analysis. *BMJ Open Diabetes Research*. 2016;4(e000184):1-8.
- Mohammed M, Sharew N. Adherence to dietary recommendation and associated factors among diabetic patients in Ethiopianteaching hospitals. *Pan African Medical Journal*. 2019;33(260):1-11.