## **Diabetes Management**

# Socio-demographic profile, asymptomatic malaria parasitaemia and glycaemic control among miled-aged and elderly type 2 diabetes mellitus patients in rural south-western Nigeria



Azeez Oyemomi Ibrahim<sup>1\*</sup>, Gbadebo Oladimeji Ajani<sup>2</sup>, Kayode Rasaq Adewoye<sup>3</sup>, Temitope Moronkeji Olanrewaju<sup>1</sup>, Eniola Ayoyemi Afolabi-Obe<sup>1</sup> & Austine Idowu Ibikunle<sup>1</sup>

**Received:** 04-Jan-2022, Manuscript No. FMDM-22-45585; **Editor assigned:** 07-Jan-2022, PreQC No. FMDM-22-45585 (PQ); **Reviewed:** 21-Jan-2022, QC No. FMDM-22-45585; **Revised:** 24-Jan-2022, Manuscript No. FMDM-22-45585 (R); **Published:** 31-Jan-2022, **DOI:** 10.37532/1758-1907.2022.12(1).284-291

### ABSTRACT

The main therapeutic goal for all type 2 diabetes mellitus (T2DM) patients is to maintain good control so as to prevent the risk of complications associated with poor control. This study determined the prevalence of poor control and its association with socio-demographics and malaria parasitaemia among middle-aged and elderly T2DM patients at a tertiary hospital in rural Southwestern Nigeria. We conducted a retrospective observational study on 250 T2DM using semi-structured interviewer administered questionnaire. Venous blood samples were collected and processed for glycated hemoglobin sugar estimation and malaria parasite detection by microscopy. Data were analyzed using SPSS version 20. Multivariate logistic regression identified the association of socio-demographics and asymptomatic malaria parasitaemia with poor control. The prevalence of poor glycemic control was 31.6% (95%CI:34.4%-45.8%). Old age, (AOR=4.868;95% CI:1.258-24.574), female genders (AOR=7.100;95% Cl:1.875-34.655), no formal education (AOR=3.447;95% Cl:1.098-21.478), presence of malaria parasitaemia (AOR=48.423; 95% CI:4.987-411.366), and higher parasite density (AOR=7.102;95% CI:1.785-15.002), were significantly associated with poor control. Health facilities should integrate screening of malaria parasitaemia into the management of T2DM patients while also exploring other barriers of poor control.

#### Introduction

Type 2 diabetes mellitus (T2DM) is the most common form of diabetes and usually characterized by sufficient insulin secretion but poor utilization by body cells, resulting in insulin resistance [1]. It constitutes about 85 to 95% of all diabetes in developed countries with a high percentage in developing countries due to increasing urbanization, sedentary lifestyles, aging population and unhealthy behavioral patterns [2,3]. The main therapeutic goal for all T2DM patients is to maintain good control so as to prevent the risk of complications associated with poor control. Good control in T2DM is defined as fasting plasma glucose level of between 80 and 110 mg/dl, or glycolated hemoglobin (HbAIC) of  $\leq$  7.0%. HbAIC is a significant indicator and marker of glycemic control over a period of about 3 months (the average red blood cell lifetime) [4].

In a longitudinal survey by Ali et al. in the United States between 2007 and 2010, the prevalence of poor glycemic control was 12.9% [5]. In sub-Saharan Africa (SSA), previous studies have revealed that, the prevalence of poor glycemic control ranged from 34 to 45% [6,7]. Socio-demographic factors, and the emerging co-occurrence of T2DM with tropical infectious diseases have been found to be associated with poor glycemic control [4,8]. This co-occurrence of T2DM and tropical infectious diseases in SSA may have substantial implications, due to the

<sup>1</sup>Department of Family Medicine, Federal Teaching Hospital, Ido-Eki, Ekiti State, Nigeri

<sup>2</sup>Department of Medicine, College of Medicine and Health Sciences, Afe Babalola University, Ado-Ekiti, Ekiti State, Nigeria

<sup>3</sup>Department of Community Health, College of Medicine and Health Sciences, Afe Babalola University, Ado-Ekiti, Ekiti State, Nigeria \*Author for correspondence: Email- Ibrahimazeez1434@gmail.com

### **KEYWORDS**

- T2DM
- asymptomatic malaria infection
- poor glycemic control
- rural

fact that malaria alone causes an estimated one million deaths annually. Despite the adoption of the global malaria elimination strategy through National Malaria Strategic Plan 2014-2020 in Nigeria, its desire effects are still far from being achieved [9]. This is probably because high risk populations of T2DM, which often comprise adults with asymptomatic malaria parasitaemia (ASM), remain undiagnosed and serve as hotspots of malaria transmission with varying intensity [10].

A study by Udoh in Nigeria showed that the prevalence of ASM among T2DM was 7.2% and 16.8% using light microscopy and Polymerace Chain Reaction (PCR) respectively. The study further revealed that poor glycemic control was significantly associated with ASM (p<0.04).

However, there is an observed paucity of data regarding the prevalence of poor glycemic control and its association with sociodemographic profile and ASM among T2DM in rural areas of Southwestern Nigeria. Data on the co-occurrence of T2DM and ASM in the same individual in rural settings are critical to enhancing the health system's preparedness towards meeting patient expectations, leading to improved health care delivery and outcomes. The present study determined the prevalence of poor glycemic control and its association with socio-demographics and ASM among T2DM in rural Southwestern Nigeria. Findings from this study would guide development of strategies to reduce the incidence of poor glycemic control and improve its case management. It would also contribute to the global elimination of ASM through case detection and treatment, in addition to integrated vector control efforts in transmission-prone areas.

### Materials and Methods

### Study area

The study was conducted at the Family Medicine clinic of Federal Teaching Hospital (FTH), Ido-Ekiti, South western Nigeria. Ido-Ekiti is located in the rural area of Ekiti State and about 30km from Ado Ekiti, its state capital. The total landmass of the community is 332 km2, with a projected population of 225,305. The majority of the populations are employed within the informal sector mainly as farmers and traders. The hospital offers secondary and tertiary care including specialist diabetic clinic to the people of its catchment area and its neighborhood states. In the study area, malaria transmission is perennial during the raining (April-October) and dry (November-March) seasons. T2DM is also a health challenge among adult populations in the state and case of poor glycemic control among patients attending the study center had been reported.

### Study design

This was a retrospective observational study of T2DM on follow up.

#### Study population

The study population comprised T2DM patients who have been receiving treatment at the study center for at least six months.

### Inclusion criteria

Consented T2DM patients who were aged 40 years and above and were on follow up for at least six months. They were also on oral antidiabetic medication (metformin, glibenclamide or both) and were  $\geq$  95% treatment adherence in the previous three months (i.e, not missing more than six doses during the period for twicedaily or thrice-daily regimen). They were also asymptomatic for malaria.

### Exclusion criteria

Respondents who were critically ill or have a major psychiatric illness and could not follow the study protocol. Also, those on anti-malaria treatment or had just completed anti malaria within two weeks prior to the recruitment of this study. Other exclusion criteria were obese patient with Body Mass Index (BMI)  $\geq$  30 Kg/m2 and hypertension (Mean Blood Pressure of  $\geq$  130/80 mmHg for two measurements) and other diabetic related complications.

### Sample size determination

Using the formula:  $n=Z2P q/d^2.14$  where n is the minimum sample size, p is the 12.9%,being the prevalence of poor control among T2DM patients on oral hypoglycemic agents with a confidence Interval of 95% at 5% margin of error. Attrition was added to allow for unexpected data losses and drop-out, a total of 250 eligible respondents were enrolled.

### Sampling technique

A systematic random sampling technique was used to recruit the 250 respondents who fulfilled the inclusion criteria. The medical records of T2DM patients on follow up at Family Medicine clinic of the study health facility, showed that in

### Socio-demographic profile, asymptomatic malaria parasitaemia and glycaemic control among miled-aged and elderly type 2 diabetes mellitus patients in rural south-western Nigeria

the year 2019, an average of 10 T2DM patients were seen daily. This translated to 50 patients per week (Monday-Friday) and 600 (sample frame) patients over a period of 12 weeks that the study was conducted. Using the formula, K=N/n, where k is the sampling interval, N is the sample frame (600) and n represented the minimum sample size 250. Therefore k was approximately 2. The first respondent on each clinic day was chosen by simple random sampling and thereafter, every 2nd respondent was chosen by systematic random sampling until the sample size of 250 was attained. A sticker was placed on each of the selected folders to avoid its resampling at the subsequent clinics.

### Data collection instruments

The two instruments for data collection were the standard interviewer administered questionnaire and data collection form. The questionnaire sought information about the respondents' socio-demographic characteristics including the duration of their diabetes. The data were collected during the raining season over a period of 4 months (June to September 2020).

### Recruitment procedure

The data were collected using a pretested interviewer semi-structured administered questionnaire which was developed by the researchers. The questionnaire was pretested on 15 T2DM patients, who were also on follow up, and were picked at random at the family medicine clinic of the Ekiti State University Teaching Hospital (EKSUTH) which is located at about 30 km from the study center. The pretesting which lasted for two days was to show the fairness of the questionnaire and its applicability. Modifications of the questionnaire were done using the feedback from the pretest and validity assessment. The questionnaire took about 10 minutes to complete. Our methodology may be reproduced by fellow researchers if they so desire.

### Clinical parameters of the respondents

**Blood pressure (B.P):** With the aid of a reliable Accosson brand of Mercury Sphygmomanometer, blood pressure of the respondents was recorded twice after about 5 minutes apart and the mean B.P of  $\leq$  130/80 mmHg was considered as controlled. The recording was done by a Senior Resident doctor.

Body Mass Index (BMI): The weight was measured to the nearest 0.1 kg and height to the nearest 0.1 cm. Normal BMI was defined

as 18.5–24.9 kg/m<sup>2</sup>, underweight as<18.5 kg/m<sup>2</sup>, overweight as 25-29.9 kg/m<sup>2</sup> and obese as  $\ge$  30.0 kg/m<sup>2</sup>.

*Glycated Hemoglobin (HbAIc):* After an overnight fast, 4 mls of blood samples were collected through the venous route into fluoride and ethylenediaminetetra-acetic acid (EDTA) immunochemically on DCA 2000; HbAIc auto analyzer using kits supplied by Boehringer (Germany) Mannheim auto analyser. Accuracy of the test result was ensured using commercially prepared standards and control samples. Glycemic level was grouped into good control if HbAIc is  $\leq$  7.0% (i.e  $\leq$  53 mmol/mol) and uncontrolled if HbAIc is>7.0% (i.e>53 mmol/mol).

Microscopy: Two blood films, one thin and one thick was made from the blood sample collected for malaria parasitaemia. The thick and thin smears were prepared on clean, dry microscope glass slides and were allowed to dry. The thin smear was fixed in methanol and both smears were stained with 2% Giemsa BDH Laboratory supplies; Poole BH 15 ITD England. The slide was then viewed under a microscope using oil immersion at 100 x magnification. Staining of the slide and parasite counting were done by a laboratory scientist of the hospital. The film was earlier viewed for the presence of parasite. A positive result means the presence of one parasite per 100 power field while a negative result means absence of parasite at 200 high power fields. Parasite density was then calculated using the formula; number of parasites over the number of leucocytes multiply by 8000 to give the number of parasites per microlitre of blood. A senior scientist was recruited to examine the slide for quality control.

### Data entry and analysis

Data collected were exported into SPPSS version 22.0 for analysis. Computations, tabulations of proportions, percentage and other summary statistics were done. Chi-square analysis was used to determine the significance of association. Mean value was compared with students t-test. Chi-square (x<sup>2</sup>) and Fisher's exact test were used to compare the proportion of categorical variables. A p-value of<0.05 was considered significant. Binary statistically regression was done to identify the variables that were significantly associated with glycemic control and such variables were exported to the multivariate logistic regression model. The strength of the association between independent and dependent

# **RESEARCH ARTICLE**

variables was measured using odds ratio and 95% confidence Interval (CI) with significant level ( p-value<0.05).

#### Ethical clearance, consideration and consent

Ethical approval for the study was received from the Ethics and Research Committee of the Institution's study center. All consented patients were thoroughly informed about the risks and advantages of the procedures. Written informed consent for the procedure and treatment was obtained from each respondent and participation was fully based on their willingness. Confidentiality and privacy were ensured throughout the study. The study was at no cost to the respondents. All patients' details have been de-identified.

### Results

The majority of the respondents, 171 (68.4%) had good glycemic control while 79 (31.6%) had poor control (TABLE 1).

In this study, there was statistically significant association between poor glycemic control and respondents' age (Chi-square  $(x^2)=22.75$ ,

p<0.05), gender ( $x^2$ =27.32, p<0.05), marital status( $x^2$ =11.922,p<0.05), occupations ffis as a ( $x^2$ =30.288, p<0.05), educations ( $x^2$ =23.746, p<0.05), income ( $x^2$ =12.982, p<0.05), and duration of diabetes ( $x^2$ =16.75%, p<0.05) (TABLE 2).

The association between poor glycemic control and ASM showed that the prevalence of poor control differed significantly between the respondents who were tested positive for ASM ( $x^2$ =70.203, p<0.05), and those with higher parasite density ( $x^2$ =70.500, p<0.05) (TABLE 3).

Using multivariate binary logistic regression for factors associated with poor control; respondents aged 61 years and above (adjusted OR=4.868; 95% CI:1.258-24.574, p=0.032).female gender (adjusted OR=7.100; 95% CI:1.875-34.655, p=0.015), lack of formal education (adjusted OR=3.447; 95% CI:1.098-21.478, p=0.047), presence of ASM parasitaemia (adjusted OR=48.423; 95% CI:4.987-411.366, p<0.001), and higher malaria parasite density (adjusted OR=7.102; 95% CI:1.785-15.002, p=0.021) were observed to be associated with poor glycemic control (TABLE 4).

TABLE 1. Prevalence of glycemic control among the respondents.					
Variable	Frequency	Percentage (%)			
	N=250				
Glycemic Control					
Poor	79	31.6			
Good	171	68.4			
Mean HbA1c ± SD(%)	7.0 ± 2.2				

TABLE 2. Association between glycemic control and socio-demographic characteristics of the respondents (N=250).

	Glycemic control				
Variable	Poor	Good	Chi-square(χ2)		
				p-value	
	n(%)	n(%)		I	
		Age group (in years)			
40-60	15 (14.7)	87 (85.3)	22.751	<0.001	
61 and above	64 (43.2)	84 (56.8)	22./51		
Mean age ± SD	62.5 ± 11.5	56.7 ± 8.6	4.872t-test	<0.001	
Gender					
Male	10 (11.1)	80 (88.9)	07.040	<0.001	
Female	69 (43.1)	91 (56.9)	27.312		
Marital status					
Married	46 (25.4)	135 (74.6)		0.003	
Separated	4 (57.1)	3 (42.9)	11.922		
Widowed	29 (46.8)	33 (53.2)			
Occupation					
Civil Servant	5 (8.2)	56 (91.8)	30.288	<0.001	

Socio-demographic profile, asymptomatic malaria parasitaemia and glycaemic control among miled-aged and elderly type 2 diabetes mellitus patients in rural south-western Nigeria

Artisan	2 (40.0)	3 (60.0)		
Farmer	15 (38.5)	24 (61.5)		
Trader	48 (47.1)	54 (52.9)		
Retiree	6 (18.8)	26 (81.2)		
Dependent	3 (27.3)	8 (72.7)		
		Level of education		
None	24 (47.1)	27 (52.9)		<0.001
Primary	26 (33.3)	52 (66.7)	22.746	
Secondary	16 (51.6)	15 (48.4)	25.740	
Tertiary	13 (14.4)	77 (85.6)		
		Domicile		
Rural	43 (34.1)	83 (65.9)	0.751	0.386
Urban	36 (29.0)	88 (71.0)	0.751	
		Income		
Low ( ≤ \$1.90 /day	54 (41.9)	75 (58.1)	12.982	<0.001
High (>\$1.90/day	25 (20.7)	96 (79.3)		
		Duration of Type 2 D	M	
< 10 years	33 (21.9)	118 (78.1)	16 756	<0.001
≥ 10 years	46 (46.5)	53 (53.5)	10.750	
Note: T-Independent t	test			

Note: I-Independent t tes

#### TABLE 3. Association between glycemic control and malaria parasitaemia in the studied respondents (N=250)

	Glycemic control			
Variable	Poor	Good		
			Chi square	p-value
	n(%)	n(%)		
Asymptomatic malaria parasitaemia				
Present	33 (91.7)	3 (8.3)	70.203	<0.001
Absent	46 (21.5)	168 (78.5)		
Parasite density				
Negative	46 (21.5)	168 (78.5)	70.500	<0.001
101-1000	13 (86.7)	2 (13.3)		
1001-2000	20 (95.2)	1 (4.8)		

### TABLE 4. Multivariate binary logistic regression analysis for factors associated with poor glycemic control among the respondents.

		1		
Variable	AOR	95% CI for AOR		
		LB	UB	p-value
		Age group (in years)		
40-60 (ref)	1.000			
61 and above	4.868	1.258	24.574	0.032
		Gender		
Male (ref)	1.000			
Female	7.100	1.875	34.655	0.015
Gender				
Married (ref)	1.000			
Separated	5.698	0.354	89.312	0.244
Widowed	6.452	0.497	123.471	0.158
Occupation				
Civil Servant (ref)	1.000			
Artisan	22.247	0.746	138.571	0.074
Farmer	15.691	0.934	114.367	0.059
Trader	6.178	0.784	52.639	0.236

Retiree	32.657	2.367	157.114	0.061
Dependent	4.978	0.241	34.993	0.452
		Level of education		
None	3.447	1.098	21.478	0.047
Primary	1.222	0.133	3.241	0.422
Secondary	0.978	0.034	2.745	0.520
Tertiary (ref)	1.000			
		Income		
Low ( $\leq$ \$1.90 /day	1.988	0.456	7.889	0.265
High (>\$1.90/day (ref)	1.000			
Duration of Type 2 DM				
< 10 years (ref)	1.000			
≥ 10 years	3.445	0.784	7.694	0.149
Asymptomatic malaria parasitaemia				
Present	48.423	4.987	411.366	<0.001
Absent (ref)	1.000			
Parasite density (u/l)				
0 (ref)	1.000			
101-1000	2.611	0.645	6.397	0.360
1001-2000	7.102	1.785	15.002	0.021
Note: ref-Reference Cate	egory; Cl-Confidence l	nterval; UB-Upper Boun	dary; AOR-Adjusted O	dd Ratio;LB- Lower

**Note:** ref-Reference Category; CI-Confidence Interval; UB-Upper Boundary; AOR-Adjusted Odd Ratio;LB- Lower Boundary

### Discussion

The study reported 31.6% as prevalence of poor glycemic control. This finding is consistent with the reports of 32.5% which was found by Ajayi and might be due to the similarity in the study design, and socio-demographic characteristics of the study respondents. However, our finding is higher than 12.9% found by Ali in the United State. This might be due to the difference in socio-economic level, diabetes management guidelines, and level of care. In the same vein, the result of our study is less than 47.0%, and 48.0%, which was found by Danguah and Yigazu respectively. The difference between our study and these other studies could be due to the variation in the clinical characteristics of the respondents and the screening tool employed.

In this study, respondent aged 61 years and above were found to be significantly associated with poor control as they were approximately five times as likely to have poor control. The finding is consistent with previous studies which found older patients having difficulty in controlling their glycemic level. This would further contribute to decreasing life expectancy in rural Nigeria. This might be due to reduction in insulin secretion and poor glucose utilization observed in older patients. Studies have shown that pancreatic beta cell function deteriorates as age increases. In contrast to this finding, the study by Kakade, found no relationship between glycemic control and age while the study by Wabha and Chang reported that there was a better improvement in the glycemic level among the older patients.

In this study, female genders have been found to be significantly associated with poor control as they were seven times as likely to have poor control. This is consistent with the findings of previous studies, but opposite to study by Yakubu. The higher prevalence of poor control in females might be due to higher natural deposit of fat contents which facilitated insulin resistance than males. In this study, respondents who had no formal education were found to be significantly associated with poor control as they were three times as likely to have poor control. This finding is consisted with reports of other studies. These studies have found that lack of formal education is associated with poor health, low glycemic diabetes knowledge and its treatment. This might result in low compliance with recommended treatment and lower continuity of care. However, study by Salaam found no relationship between poor control and level of education.

In this study, the respondents who were tested positive for ASM parasitaemia were 48 times as likely to have poor control. This is consistent with previous studies. These collective findings in our study and the other studies suggest that adult T2DM patients were potential reservoirs of malaria. Though, previous studies have not been able to define the actual reason for poor control in respondents with the presence of ASM, the risk increases with increase in the density of the Socio-demographic profile, asymptomatic malaria parasitaemia and glycaemic control among miled-aged and elderly type 2 diabetes mellitus patients in rural south-western Nigeria **RESEARCH ARTICLE** 

parasite and may be a sign of biology plausibility. The implication of this finding is that in rural setting, where malaria is threatening the life of the populace, the proportion of people with poor control may further worsen. However, large community based studies are required to clarify fully the relationship between ASM parasitaemia and glycemic control among T2DM patients.

#### Conclusion

Nearly one-third of the respondents had poor glycemic control. Old age, female gender, lack of formal education, presence of ASM, and higher parasite density were significantly associated with poor control. Health facilities should integrate screening of malaria parasitaemia into the management of T2DM patients whose glycemic level were not control despite treatment compliance, while also exploring other barriers of poor control.

### Limitations

Firstly, this study is cross sectional, and therefore, cannot ascertain the causal association between the outcome variables and the potential determining factors. Also, the smaller sample size may limit the generalization of the study findings to a larger population of T2DM in rural Southwestern Nigeria. Nevertheless, the use of HbAIC, which is the gold standard index of control, validates this study.

### **Consent to Participate**

As applicable in the ethical clearance above.

### Availability of Data and Materials

The datasets for this study would be made available from the corresponding author on a reasonable request

### **Declaration of Conflicts of Interest**

The authors declare that they have no conflicts of interest.

### Funding

The researcher received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

### Authors' Contribution

AOI-Conceptualization of the study designed the study protocol, data acquisition and analysis and drafted the initial manuscript. GOA-Critically revised the protocol for methodological and intellectual content. KRA, OTM, EAA, AII-Literature review, data analysis and review of manuscript for intellectual content. All the authors read and approved the final version of the manuscript prior to submission.

### Acknowledgment

The authors expressed profound gratitude to the management of the Federal Teaching Hospital Ido-Ekiti for providing conducive atmosphere for the conduct of this research. Appreciation goes to the resident doctors and nurses at the Family Medicine Department.

### References

- Boden G, Shulman GI. Free Fatty Acids in Obesity and Type 2 Diabetics: Defining Their Role in the Development of Insulin Resistance and Beta Cell Dysfunction. *Eur J Clin Invest.* 32:14-23 (2002).
- 2. Roman SH, Harris MI. Management of Diabetes Mellitus from a Public Health Perspective. *Endocrinol Metab Clin North Am*. 26(3): 443-74 (1997).
- Digssie A, Abebaw S, Achaw A, et al. Level of Glycemic Control and Its Associated Factors among Type 2 Diabetics Patients in Debra Tabor General Hospital, Northwest Ethiopia. *Metab Open*. 8(1):100056 (2020).
- 4. Buell C, Kermah D, Davidson MB. Utility of

Aic for Diabetes Screening in the 1999- 2004 Nhanes Population. *Diabetes Care*. 30(3): 2233-5 (2007).

- Ali MK, Bullard KM, Imperatore G, et al. Characteristics Associated with Poor Glycemic Control among Adults with Self-reported Diagnosed Diabetes. National Health and Nutrition Examination Survey, United States, (2007).
- 6. Sheleme T, Mama G, Tamiru S. Predictors among Adult Diabetes Mellitus Attending Mettu Karl Referral Hospital, Southwest Ethiopia: A Prospective Observational Study. *Diabet Therapy*. 11:1775-94 (2020).
- 7. Okafor CI, Ofoegbu EN. Control of Goal of Cardiometabotic Risk Factors among

Nigerians Living with Type 2 Diabetes Mellitus. *Niger J Clin Pract.* 15(2): 15-8 (2012).

- Lopez AD, Mathers CD, Ezzati M, et al. Global and Regional Burden of Disease and Risk Factors. 2001 Systematic Analysis of Population Health Data. *Lancet.* 367(9524): 1747:57 (2006).
- 9. Sturrock HJ, Hsiang MS, Cohen JM, et al. Targetting Asymptomatic Malaria Infections: Active Surveillance in Control and Elimination. *PLoS Med.* 10 (6):13-21 (2013).
- 10. Udoh BE, Iwalokun BA, Etukumana E, et al. Asymptomatic Falciparum Malaria and Its Effect on Type 2 Diabetes Mellitus Patients in Lagos, Nigeria. *Saudi J Med Med Sci.* 8: 32-40 (2019).