International Journal of Health Sciences and Research
www.ijhsr.org ISSN: 2249-9571

Original Research Article

Age and Gender Specific Prevalence among Non-Insulin Dependent Diabetes Mellitus (Type II) and its Correlation with HbA1c % level, A Hospital-Based Cross-Sectional Study

Roshina Bano[1], Prof. Anisa M Durrani[2]

[1]Research Scholar, [2]Professor
Department Of Home Science, Faculty of Agricultural Sciences, AMU Aligarh.

Corresponding Author: Roshina Bano

ABSTRACT

In perspective of whether HbA1c% level may fluctuate with the gender and age of patients, the present investigation was carried out with the aim to estimate gender and age occurrence of type 2 diabetes and association of HbA1c% level among male-female of different age groups. The hospital-based cross-sectional descriptive study was carried out among 160 patients of diabetes aged 20 years and above visiting outpatients clinic' over a period of 6 months from Aug17 to Jan18 at endocrinology department of Jawaharlal Nehru medical college and Hospital, Aligarh. A predesigned pretested structured questionnaire cum interview schedule was used to collect data. Diagnostic criterion was based on (WHO/IDF) 2006 for diabetes. HbA1c% level is used as an indicator of glycemic controls among 160 patients with non-insulin diabetes mellitus. An independent sample t-test, one-way ANOVA and Spearman rank correlation test was applied using IBM SPSS version 21.0. More than fifty percent patients were female 106 (66.2%) than that of males 54 (33.8%) among total patients. Although there was the significant difference between ages (P=<0.05) but no significant difference (P=>0.05 NS) was demonstrated by HbA1c% level among both genders and also no significant difference in the HbA1c % level of patients between different age groups, F (2,157) =1.57, p>0.05. Spearman rank correlation coefficient was found to be R= (-0.99), P>0.05 which implies that there was a mild inverse correlation between actual age and HbA1c% level. So age must be considered while diagnosing HbA1c% level for the identification of diabetes.

Keywords: prevalence, Diabetes mellitus, HbA1c% level, Gender, Age

INTRODUCTION

Non-insulin diabetes mellitus also known as type II diabetes is one of the foremost cause of the mortality and morbidity around the world. [1] The age-standardized prevalence of adult's diabetes was 422 million in 2014 as compared 108 million in 1980. It specifies that the global burden of diabetes mellitus from 1980 has almost doubled and the prevalence in adult population increased from 4.7% to 8.5%. [7] Globally, 425 million people with diabetes were estimated in the year 2017 out of which 72.9 million are from India, implying that the figure of individuals with diabetes is growing day by day and in every country with the highest increase recorded in low and middle-income countries. [1] Diabetes mellitus increases the chances to develop some diseases such as coronary heart disease (CHD), stroke, peripheral arterial disease, nephropathy, retinopathy, neuropathy and cardiomyopathy. [3,35] The consequence is high in developing nations than developed nations. It is expected that, even though there will be a 42% rise in diabetes occurrence in developed nations, developing nations will go through 170% rise between 1995 and 2025. [2,3] As per world health organization this dynamic

increment in the prevalence of diabetes linked with the possibly adjustable factors such as lifestyle modification, excess weight, inactive life, increased consumption of alcohol, smoking and unhealthy dietary habits. Evaluating the prevalence of diabetes and the number of individuals influenced by diabetes now and in future is essential to take into account national planning and allocation of resources. Since the proportion shifts from nation to nation, state to state, races and cultural gatherings. [4] American Diabetes Association guidelines of 2016 have consolidated HbA1c% level as a diagnostic standard for diabetes mellitus. [5] Diabetes is diagnosed by estimating glucose in a blood test taken while the patient is in a fasting state, or 2 hours after a 75 g oral load of glucose has been taken. In addition, diabetes can also be analyzed by estimating Glycosylated hemoglobin (HbA1c% level), regardless of whether the patient is in fasting state or not. [6-7] Glycated hemoglobin (HbA1c% level) is a type of hemoglobin to which glucose is bound. HbA1c% level is measured primarily to discover the three-month average plasma glucose concentration because the lifespan of a red blood cell is four months (120 days). However, since red blood cells do not all undergo lysis at the same time, HbA1c% level is taken as a limited measure of three months. [33] As HbA1c% level testing can be performed at any time of the day and without any exceptional patient planning (for example, fasting is not compulsory) as well as gives more precise data regarding the disease and the patient, it provides better comfort for patients and healthcare suppliers in comparison to the oral glucose tolerance test or taking fasting plasma glucose measurements. [8,9] Based on this, it has been recommended that HbA1c% level may perform like a better indicator for glucose control in diabetic patients in comparison to fasting blood sugar levels. [10,11] In spite of this, it is vital to take age, ethnicity, anemia/hemoglobinopathies(and other different diseases for which HbA1c% level might be inadequate standard for the determination of type 2 diabetes) into consideration while using the HbA1c% level to diagnose diabetes. [12,13] For ideal blood glucose control, American Diabetes Association (ADA) targeted <7% Hb [14] and <6.5% of Hb further suggested by the American Association's Clinical endocrinologists (AACE) [15] shown in table 1. The measurement of HbA1c% level was observed to be beneficial over blood glucose levels in anticipating the risk of developing diabetes or heart diseases. [16]

Additionally, in the diagnosis of type II diabetes, more studies are therefore necessary to upgrade more suitable criteria for Glycosylated hemoglobin. Besides these recent studies of china in 2016 reported positive correlation between levels of HbA1c % and patient age, it means HbA1c% level values increase with age. [17] However till date no such studies has been done, in the association of HbA1c% level and gender, age in Aligarh city. In perspective of whether HbA1c% level may fluctuate with the gender and age of patients, the present investigation was carried out with the aim to estimate gender and age occurrence of type 2 diabetes and association of HbA1c% level among male-female of different age groups due to outstanding variation in HbA1c% level between genders of different age. [17]

Table I Glucose Testing and Interpretation [34]

Normal	High Risk for Diabetes	Diabetes
FPG <100 mg/dL	IFG FPG ≥100-125 mg/dL	FPG ≥126 mg/dL
2-h PG<140 mg/dL	IGT 2-h PG ≥140-199 mg/dL	2-h PG ≥200 mg/dL Random PG ≥200 mg/dL + symptoms
A1C<5.5%	5.5 to 6.4% For screening of prediabetes[a]	≥6.5% Secondary[b]

Abbreviations: A1C = hemoglobin A1C; FPG = fasting plasma glucose; IFG = impaired fasting glucose; IGT = impaired glucose tolerance; PG = plasma glucose.

[a]A1C should be used only for screening prediabetes. The diagnosis of prediabetes, which may manifest as either IFG or IGT, should be confirmed with glucose testing.

[b]Glucose criteria are preferred for the diagnosis of DM. In all cases, the diagnosis should be confirmed on a separate day by repeating glucose or A1C testing. When A1C is used for diagnosis, follow-up glucose testing should be done when possible to help manage DM.

METHODS

The hospital-based cross-sectional descriptive study was carried out among 160 patients of diabetes mellitus (DM) aged 20 years and above visiting outpatients' clinic over a period of 6 months from August 2017 to January 2018 at endocrinology department of Jawaharlal Nehru Medical College and Hospital, Aligarh. Aligarh city is a part of the northern India and district of Uttar Pradesh. Uttar Pradesh is the most populous state in India with the population of 199,812,341. Aligarh city constitutes of 3,650 sq.km area with the population of around 36.7 lakhs among these around 19.5 lakhs are males while 17.2 lakhs are females. [18] The inclusion criteria of patient for the study were as follows: (i) Only diabetic male-female (2). Age 20 years and above (3). Diabetic patients who are willing to participate (4). Regular visitor of JNMC for checkups (5). Patients from different socioeconomic background.(6). A resident of Aligarh city, India for >5 years. Exclusion criteria was: pregnant women and hospitalized diabetic patients. Age group of patients was categorized into three categories as per Hurlock division of adulthood [19] (1). Early adulthood (20-39) years. (2). Middle adulthood (40-59) year (3). Late adulthood (60 and above). Prevalence of diabetes among adults from previous data was found to be 11.3%. [20] A sample size of 160 was calculated for the diabetic by using the simplified sample size formula for proportions $n=4pq/ l^2$ that is also more useful for medical or clinical research investigations [21] with 5 % relative error. Stratified random sampling technique was used to select study subjects because of the heterogeneous population. Ethical clearance for conducting the study was approved by the Institutional Ethics Committee, Jawaharlal Nehru Medical College& Hospital, Aligarh Muslim University, Aligarh. An informed verbal consent was taken from all the patients. A predesigned pretested structured questionnaire cum interview schedule was used to collect data regarding demographic details, anthropometry, medical history, and detailed dietary pattern which includes dietary intake and frequency of food consumption of participants. Both quantitative and qualitative data obtained from the study. Blood sugar level including fasting blood sugar (FBS), post-prandial (PP), and glycosylated hemoglobin (HbA1c %) level was recorded from the case history of office records. Diabetes mellitus was defined according to the [22] Recommendations as FBS ≥126 mg/dl or oral glucose tolerance test OGTT2 ≥200 mg/dl. HbA1c % level is used as an indicator of glycemic controls among overall patients with non-insulin diabetes mellitus. HbA1c % level was categorized as per ICMR guidelines [23] of <7 for ideal control, 7-8 for satisfactory control and >8 for unsatisfactory glycemic control.

Statistical analysis: Data was tabulated and statistical analysis was done using statistical package of IBM SPSS software version 21.0. Mean (revealed as mean ± SEM), frequencies and the proportion were computed for continuous and categorical variables under descriptive statistics. An independent sample t-test was used to test one variable comparison among two groups and for multiple groups' comparison analysis of one-way ANOVA was used. Correlation analysis of separate variables was performed with Spearman rank correlation analysis. A value of $P<0.05$ was considered to imply a statistically significant difference.

RESULTS

As shown in table II, More than fifty percent patients were female 106 (66.2%) than that of males 54 (33.8%) among total patients and the mean age of male and female were 52.6±1.5 and 48.9±0.9 respectively. Mean HbA1c % level among male and female were recorded 8.5±0.2 and 8.5±0.1 respectively. Although there was the significant difference between ages ($P= < 0.05^{*)}$ but no significant difference ($P= >0.05^{NS\ *)}$ was demonstrated by HbA1c % level among both genders.

Table II: Comparison of HbA1c levels of different gender subjects.

Groups	Frequency	Mean age	Mean HbA1c%
Male	54 (33.8%)	52.6±1.59	8.51±0.26
Female	106 (66.2%)	48.9±0.94	8.50±0.19
t-value		2.12	0.82
P- value		$< 0.05^{*}$	$>0.05^{NS}$

*All data are presented as the frequency, mean ± standard error of mean .comparison of HbA1c % level and age between male and female was done with independent sample t-test. NS = no significant (P>0.05), *P<0.05, significant at 5%*

Table III: Comparison of HbA1c%levels across different age groups:

Distribution of control of HbA1c % Among Male-Female Diabetics Of Different Age Groups						
Sex of Patients			**Age group of Patients**			**Total**
			20-39	**40-59**	**60 and Above**	
Male	HbA1c % level control	Ideal	0 (.0%)	4 (36.4%)	7 (63.6%)	11 (20.4%)
		Satisfactory	2 (15.4%)	7 (53.8%)	4 (30.8%)	13 (24.1%)
		Unsatisfactory	3 (10.0%)	19 (63.3%)	8 (26.7%)	30 (55.6%)
	Total		5 (9.3%)	30 (55.6%)	19 (35.2%)	54 (100.0%)
Female	HbA1c % level control	Ideal	6 (20.7%)	20 (69.0%)	3 (10.3%)	29 (27.4%)
		Satisfactory	4 (17.4%)	11 (47.8%)	8 (34.8%)	23 (21.7%)
		Unsatisfactory	3 (5.6%)	41 (75.9%)	10 (18.5%)	54 (50.9%)
	Total		13(12.3%)	72 (67.9%)	21 (19.8%)	106(100.0%)
	%Within total patients		18(11.2%)	102(63.8%)	40 (25.0%)	160 (100.0%)

All data are presented in frequencies and proportion glycemic control (HbA1c % level) among male female of different age groups.

Descriptive analysis estimated that most of patients 102 (63.8%) came under the age group of 40-59 (middle adulthood) as categorized by EB Hurlock19 and 40 (25.0%) of diabetics were in the age group of 60 and above (late adulthood) and rest 18 (11.2%) were in the age group of 20-39 (early adulthood) among all. Highly prevalent cases of both male and female diabetics were high in the middle age group followed by late adulthood and early adulthood. Unsatisfactory control of (HbA1c>8%) was high in male (55.6%) than female (50.9%) as shown in Table III. Analysis of one-way ANOVA was used in all three age groups' comparison, with respect to HbA1c % level. HbA1c % level test results of post hoc tests for all age groups are shown in Table IV. The results indicate that there was no significant difference in the HbA1c % level of patients between different age groups, F (2,157) =1.579, p>0.05. A homogeneous value between all three groups was almost similar which is analyzed by 0.05 % significance value. Spearman rank correlation coefficient was found to be R=-0.99, P>0.05 which implies that there was a mild inverse correlation between actual age and HbA1c% level as shown in Table V.

Table: IV: Post Hoc Tests

Multiple Comparisons						
HbA1c % level control Tukey HSD						
(I) Age group of Subjects	(J) Age group of Subjects	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
20-39	40-59	-.353	.214	.227	-.86	.15
	60 and Above	-.200	.237	.677	-.76	.36
40-59	20-39	.353	.214	.227	-.15	.86
	60 and Above	.153	.156	.590	-.22	.52
60 and Above	20-39	.200	.237	.677	-.36	.76
	40-59	-.153	.156	.590	-.52	.22

Table: V: Spearman Rank Correlation Coefficient Test

Correlations				
			Actual age of patients	Actual HbA1c% levels
Spearman's rho	Actual age of patients	Correlation Coefficient	1.000	-.099
		Sig. (2-tailed)	.	.215
		N	160	160
	Actual HbA1c% levels	Correlation Coefficient	-.099	1.000
		Sig. (2-tailed)	.215	.
		N	160	160

DISCUSSION

Age and gender both are non-modifiable risk components for type 2 diabetes beyond person's control. As the age increases the risk of diabetes as well increases significantly. Usually, type 2 diabetes happens in middle-aged adults, most frequently after age 45. [24] Globally the prevalence of diabetes in females (8.4%) is assessed to be somewhat lower than males (9.1%). the number of diabetic individuals is high in the working age of (20-64 years) than the 65-99 years. [1] The findings of the present examination suggest that more noteworthy consideration ought to be given to patient gender and age while choosing HbA1c % level as the foundation in diabetes screening, as has been accounted for in past investigations of some researchers. [3,25-29] The overall prevalence of diabetes was higher in women's 106 (66.2%) than men's 54 (33.8%). Similar results are also reported by the researcher in Nigeria, India and Zambia regarding gender wise prevalence of diabetes. [3,30,31] in both genders, the prevalence of diabetes was highest 102(63.8%) in the age groups of 40-59 years called middle adulthood and lowest 18(11.2%) called early adulthood in the 20-39 years age groups. this finding is consistent with the observation reported by Ekpenyong et al ,2012. [3] Overall unsatisfactory control of (HbA1c>8%) was significantly higher in male (55.6%) than that in female (50.9%). Similar finding also reveals in the population-based study of Korea by Ma et al., 2016 and Seo et al., 2018. [26,27] but in middle adulthood (40-59) years, females show more unsatisfactory glycemic control (75.9%) than males (63.3%). These findings are contrary to findings reported by Ma et al., 2016. [26] The present study also depicts that significant difference between ages and similar results reported by the researcher of Zambia in 2016. [31] but the insignificant difference was noted by HbA1c% level among both genders the similar findings reported by cross-sectional hospital based in Zambia. [31] Most importantly, the current study revealed mild inverse correlation recorded between actual age and HbA1c% level means Glycosylated hemoglobin decreased slightly as age rose, this finding is different with the observation reported in the UK study [32] in which there is no significant positive relationship with age for any of the groups and other findings are in agreement with our findings there was a statistically significant but weak negative correlation between HbA1c% level and age. [31] As observed in this study, after comparing HbA1c% level test results for all age groups are shown in table III that there was no significant difference in the HbA1c% level of patients between different age groups. Similar findings reported by a study conducted in China [26] in which HbA1c% levels in different age groups was not significant ($p>0.05$).

CONCLUSION

This Research concluded that HbA1c % level is a consistent marker of the glycemic status of a person. The present investigation obviously indicates that the correlation between Glycosylated hemoglobin (HbA1c % level) and age among both genders in Aligarh population which represents HbA1c concentration fluctuates through different age groups and sex. In this manner, for the identification of diabetes, we recommend that age and gender must be considered while diagnosing HbA1c % level. Intervention programs should be based on lifestyle modification.

REFERENCES

1. Atlas ID. In., 8th edn. Brussels, Belgium: International Diabetes Federation; 2017. URL: https:// http://www.diabetesatlas.org
2. King H, Aubert RE, Herman WH. Global burden of diabetes, 1995–2025: prevalence, numerical estimates, and projections. Diabetes care. 1998 Sep 1;21(9):1414-31.
3. Ekpenyong CE, Akpan UP, Ibu JO, Nyebuk DE. Gender and age specific prevalence and associated risk factors of type 2 diabetes mellitus in Uyo metropolis, South Eastern Nigeria. Diabetologia Croatica. 2012 Mar 1;41(1).

4. World Health Organization. Screening for type 2 diabetes: report of a World Health Organization and International Diabetes Federation meeting. http://www.who.int/diabetes/publications/en/screening_mnc03.pdf
5. American Diabetes Association. (2016). Standards of medical care in diabetes *Diabetes Care*. 2016; 39(suppl 1):S1-S106. Retrieved from http://www.ndei.org/ADA-2013-Guidelines-Criteria-Diabetes-Diagnosis.aspx.html
6. World Health Organization. Use of glycated haemoglobin (HbA1c) in the diagnosis of diabetes mellitus. Abbreviated report of a WHO consultation 2011. Geneva: World Health Organization. 2013.
7. World Health Organization. Global report on diabetes. World Health Organization; 2016.
8. Rohlfing CL, Little RR, Wiedmeyer HM, England JD, Madsen R, Harris MI, Flegal KM, Eberhardt MS, Goldstein DE. Use of GHb (HbA1c) in screening for undiagnosed diabetes in the US population. Diabetes care. 2000 Feb 1;23(2):187-91.
9. Kumpatla S, Aravindalochanan V, Rajan R, Viswanathan V, Kapur A. Evaluation of performance of A1c and FPG tests for screening newly diagnosed diabetes defined by an OGTT among tuberculosis patients-a study from India. Diabetes research and clinical practice. 2013 Oct 1;102(1):60-4. (india, 2011)
10. Selvin E, Steffes MW, Zhu H et al. Glycated hemoglobin, diabetes, and cardiovascular risk in nondiabetic adults. N Engl J Med. 2010 Mar 4;362(9):800-11.
11. BICESCU G. Glycated hemoglobin, diabetes, and cardiovascular risk in nondiabetic adults. Maedica. 2010 Jan;5(1):80.
12. Davidson MB, Schriger DL. Effect of age and race/ethnicity on HbA1c levels in people without known diabetes mellitus: implications for the diagnosis of diabetes. Diabetes research and clinical practice. 2010 Mar 1;87(3):415-21.
13. Yang L, Shen X, Yan S, Yuan X, Lu J, Wei W. HbA1c in the diagnosis of diabetes and abnormal glucose tolerance in patients with Graves' hyperthyroidism. Diabetes research and clinical practice. 2013 Jul 1;101(1):28-34.
14. American Diabetes Association. Implications of the United Kingdom prospective diabetes study. Diabetes care. 2003 Jan 1;26(suppl 1):s28-32.
15. American Association of Clinical Endocrinologists. The American Association of Clinical Endocrinologists medical guidelines for the management of diabetes mellitus: the AACE system of intensive diabetes self-management-2002 update. Endocr Pract. 2002;8(1):40-82.
16. Wareham NJ, Pfister R. Diabetes: glycated hemoglobin is a marker of diabetes and CVD risk. Nature Reviews Cardiology. 2010 Jul;7(7):367.
17. Ma Q, Liu H, Xiang G, Shan W, Xing W. Association between glycated hemoglobin A1c levels with age and gender in Chinese adults with no prior diagnosis of diabetes mellitus. Biomedical reports. 2016 Jun 1;4(6):737-40.
18. Census of India. (2011). Planning Commission. Ministry of Home Affairs: Government of India Retrieved from. http://www.censusindia.gov.in/2011census/PCA/PCA_Highlights/pca_highlights_file/India/Chapter-1.pdf
19. Hurlock, E.B. Developmental Psychology: A Life-Span Approach.4th ed. New York: McGraw-Hill (1980).
20. National family health survey (NFHS 4). (2016).District factsheets. India Retrieved from http://rchiips.org/NFHS/pdf/NFHS4/India.pdf
21. Singh AS, Masuku MB. Sampling techniques & determination of sample size in applied statistics research: An overview. International Journal of Economics, Commerce and Management. 2014 Nov; 2(11):1-22.
22. World Health Organization. Definition and diagnosis of diabetes mellitus and intermediate hyperglycaemia: report of a WHO/IDF consultation. (2006)
23. Indian Council of Medical Research (ICMR). (2005). Targets for Control of Diabetes: Guidelines for Management of Type 2 Diabetes. Retrieved from http://icmr.nic.in/guidelines_diabetes/section4.pdf
24. American Heart Association. (Aug 30, 2015). Understand Your Risk for Diabetes. Retrieved from http://www.heart.org/en/health-

topics/diabetes/understand-your-risk-for-diabetes
25. Bae JC, Suh S, Jin SM, Kim SW, Hur KY, Kim JH, Min YK, Lee MS, Lee MK, Jeon WS, Lee WY. Hemoglobin A1c values are affected by hemoglobin level and gender in non-anemic Koreans. Journal of diabetes investigation. 2014 Jan;5(1):60-5.
26. Ma Q, Liu H, Xiang G, Shan W, Xing W. Association between glycated hemoglobin A1c levels with age and gender in Chinese adults with no prior diagnosis of diabetes mellitus. Biomedical reports. 2016 Jun 1;4(6):737-40.
27. Seo JY, Hwang SS, Kim JH, Lee YA, Lee SY, Shin CH, Yang SW. Distribution of glycated haemoglobin and its determinants in Korean youth and young adults: a nationwide population-based study. Scientific reports. 2018 Jan 31;8(1):1962.
28. Yang L, Shen X, Yan S, Xu F, Wu P. The effectiveness of age on H b A 1c as a criterion for the diagnosis of diabetes in C hinese different age subjects. Clinical endocrinology. 2015 Feb;82(2):205-12.
29. Inoue M, Inoue K, Akimoto K. Effects of age and sex in the diagnosis of type 2 diabetes using glycated haemoglobin in Japan: the Yuport Medical Checkup Centre study. PloS one. 2012 Jul 5;7(7):e40375.
30. Narayanan, M. (2017). Correlation of HbA1C levels with average Estimated blood Glucose levels in improvement of Diabetes Management, 13(3), 205–210
31. Musenge EM, Manankov A, Michelo C, Mudenda B. Relationship between glycated haemoglobin and fasting plasma glucose among diabetic out-patients at the University Teaching Hospital, Lusaka, Zambia. Tanzania Journal of Health Research. 2016; 18(3).
32. Wiener K, Roberts NB. Age does not influence levels of HbA1c in normal subject. Qjm. 1999 Mar 1; 92(3):169-73.
33. Wikipedia contributors. (2018, August 25). Glycated hemoglobin. In Wikipedia, The Free Encyclopedia. Retrieved 16:19, September 5, 2018, from https://en.wikipedia.org/w/index.php?title=Glycated_hemoglobin&oldid=856440755
34. Handelsman Y, Bloomgarden ZT, Grunberger G, Umpierrez G, Zimmerman RS, Bailey TS, Blonde L, Bray GA, Cohen AJ, Dagogo-Jack S, Davidson JA. American Association of Clinical Endocrinologists and American College of Endocrinology–clinical practice guidelines for developing a diabetes mellitus comprehensive care plan–2015. Endocrine Practice. 2015 Apr; 21(s1):1-87.
35. Grundy SM, Benjamin IJ, Burke GL, Chait A, Eckel RH, Howard BV, Mitch W, Smith Jr SC, Sowers JR. Diabetes and cardiovascular disease: a statement for healthcare professionals from the American Heart Association. Circulation. 1999 Sep 7; 100(10):1134-46.

How to cite this article: Bano R, Durrani AM. Age and gender specific prevalence among non-insulin dependent diabetes mellitus (type II) and its correlation with HbA1c % level, a hospital-based cross-sectional study. Int J Health Sci Res. 2018; 8(11):102-108.

******