

Analyzing Oral Health Knowledge, Attitude and Awareness among Diabetic Adults in the United States

Manju Natarajan*

BDS, MS - Master of Science in Health Sciences, Merrimack College, Massachusetts, USA

*Corresponding author

Manju Natarajan, BDS, MS - Master of Science in Health Sciences, Merrimack College, Massachusetts, USA, E-mail: Manju.parthiban@gmail.com

Submitted: 08 June 2018; Accepted: 15 June 2018; Published: 27 June 2018

Abstract

Diabetes is a serious health issue as it leads to heart disease and other complications. The link between diabetes and oral disease is proven in many scholarly literatures. The bi-directional relationship between the two is well known among healthcare academia, and its professional community.

Purpose: The goal of this study is to understand how much of this awareness and knowledge has reached common people suffering from diabetes. Specifically, this study ventures to understand if the diabetics are aware of the oral disease complications and their attitude towards oral health. The results of this study could aid in developing health promotion programs targeting diabetics to positively influence their quality of life.

Methodology: Thirty (30) diabetics who are members of the Young Men's Christian Association (YMCA) in Massachusetts, USA were recruited through convenient sampling method. Responses to a series of questions relating to demographic, symptomatic, attitude, oral hygiene practices and awareness-level were gathered through a two-page questionnaire. Data analysis was done using statistical tools such as descriptive analysis, relative frequency measures and correlation analysis.

Results: 67% of the respondents were aware of the link between oral health and diabetes; 87% had positive attitude towards oral health; minimum of 73% had no oral symptoms; only 27% conformed to dentist recommended everyday oral hygiene practices; Correlation of oral hygiene practices and less symptomatic measure had an R value of 0.82.

Conclusion: A positive attitude towards oral health and above average awareness of the link between oral health and diabetes did not translate to regular oral hygiene practices. The correlation analysis between oral symptoms and oral hygiene practices showed that higher the number of oral hygiene practices, the lesser the number of symptoms this group had. Hence, reinforcing the practices of oral hygiene through diabetic intervention programs could improve the quality of life for diabetics.

Keywords: Diabetes, Relationship with Oral Health, Diabetes and Oral Health, Oral Health Link to Diabetes

Introduction

Overview of Diabetes

According to World Health Organization (WHO), diabetes is defined as a chronic disease that occurs either when the pancreas does not produce enough hormones regulating blood sugar called insulin or when the body cannot effectively use the insulin it produces [1]. There are two types of diabetes, Type 1 and Type 2. Type 1 diabetes is a chronic autoimmune disease in which the beta cells in the pancreas create little to no insulin, and accounts for 5% to 10% of all diabetes cases [2]. Type 2 diabetes accounts for 85% to 90% or more of diabetes cases and is one of the most common chronic diseases, as well as one of the leading causes of death and disability in the U.S [3]. In 2015, 84.1 million Americans age 18 and older had prediabetes [4].

Increased blood sugar known as Hyperglycemia is a common effect of uncontrolled diabetes and over time leads to serious damage to many of the body's systems, especially the nerves and blood vessels [1]. Diabetes complications include heart disease, blindness and other eye problems, kidney diseases and amputation [3]. Diabetes diagnosed during pregnancy is called Gestational diabetes and its complications are pre-eclampsia (pregnancy induced high blood pressure), birth defects, birth related trauma and developing type 2 diabetes later in life [5].

Among adults over 18 years, the global prevalence of diabetes has risen from 4.7% (108 million) in 1980 to 8.5% (422 million) in 2014 [6]. The prevalence of Diabetes in the United States is equally alarming. A total of 25.8 million people which is about 8.3% of population in the U.S are affected by Diabetes and over 7 million are unaware that they suffer from the disease [7,8]. In 2015, the 7th leading cause of death in the United States was Diabetes, with 79,535 death certificates listing it as the underlying cause of death, and a

total of 252,806 death certificates listing diabetes as an underlying or contributing cause of death [4]. In 2015, an estimated 1.5 million new cases of diabetes (6.7 per 1,000 persons) were diagnosed among U.S adults aged 18 years or older of which more than half of these new cases were among adults aged 45 to 64 years, with equal split between men and women [3].

Overview of Oral Health

When it comes to oral health, aspiration towards preventive oral health measures is not consistent with actions taken. For instance, in an oral health and well-being survey of 14,962 respondents, it was found that 77% of adults say they plan to visit the dentist within the following 12 months but only 37% actually visited a dentist within the past 12 months [9]. Between 2011 and 2014, 31.6% of adults aged 20-44 were with untreated dental caries and in 2015, 64% of 18-64 years old adults visited a dentist [5]. Among adults aged 18-64, about three-quarters had very good or good oral health, 17% had fair oral health, and 7% had poor oral health [5]. Adults aged 18-64 with a bachelor's degree (39%) had a better oral health status than adults with less than a high school diploma (20%) [5]. The most common reason people (59%) quoted for not visiting a dentist was cost [9]. Hence, it is very clear that the oral health status is strongly associated with socio-economic status of the population.

Oral Health, Well-Being and Diabetes

The health of the teeth, the mouth, and the surrounding craniofacial (skull and face) structures is central to a person's overall health and well-being as oral cavity is the portal of entry and site of disease for microbial infections that affect general health status [10,11]. Ability to speak, smile, taste, chew, swallow and make facial expressions depend on good oral health [11]. Many systemic diseases have oral manifestations which may be the initial sign of clinical disease and serve to inform clinicians and individuals of the need for further assessment [11]. Due to the strong association between oral health and general well-being, it is one of the objectives of Healthy People-2020. Adults with diabetes (29%) were almost twice as likely as adults without diabetes (16%) to have worse oral health status than others the same age [3].

Past Studies on Oral Health Knowledge and Awareness among Diabetics

A six-year survey analysis by CDC from the Behavioral Risk Factor Surveillance System (BRFSS), concluded that the estimates for dental visits during the preceding 12 months among adults with diabetes did not reach the targets set by the national objective for 2010 [12]. The report further underscored the need to increase awareness of oral health in diabetes care. In another survey of 111 respondents with diabetes, respondents agreed that they get information about diabetes from multiple sources, including family, friends and health care providers; however they demonstrated very limited knowledge about the link between diabetes and periodontal diseases [13].

In a 2008 study conducted to assess the knowledge of 101 diabetic patients about the risk of periodontal disease, their attitude toward oral health and their oral health-related quality of life, it was found that only 33% were aware of their increased periodontal disease risk and only 43% reported seeing a dentist in the preceding 12 months [14].

Methodology

Participants

Diabetic patients who are members of the Young Men's Christian Association (YMCA), also known as the Y was the target organization to recruit about 30 participants. The sampling method used in this study was convenient sampling which is a type of non-probability sampling. All participants were recruited from the Y located in the state of Massachusetts with the permission of the individual site's Chief Executive Officer (CEO).

Both male and female participants suffering from either Type-1 or Type-2 diabetes aging 18 years and older were recruited. All Y diabetic participants are either part of any of the general program or specialized programs such as diabetes prevention program. The participants had at least one natural tooth and had diabetes for at least six months to ensure they have experienced some of the symptoms of oral diseases. Patients who were in the medical profession (doctors, nurses, medical assistants etc.) Were excluded from the study as their knowledge about the oral disease might skew the results. In addition, patients who cannot read or write and who are not physically able to provide written feedback were excluded from this study.

Measures

The intent of the study was to contribute to the future research in the design of an effective intervention strategy to improve oral health quality of life among diabetic patients. The different measures that were tested in this study provided a baseline knowledge and awareness level of patients with diabetes which could possibly aid in the gap identification for the current and future diabetes interventions. The information in this study was collected through a two-page questionnaire with simple multiple choice and yes or no type questions. The different measures are described in the passages below.

Demographic Measures

The measures of demographic in this study are broadly categorized into basic information, economic status and length of diabetes related information. Basic demographic information includes age, sex and race. Economic status information collected includes education level and family income. The basic and economic status demographics helped in the analysis of any factors that might contribute to surplus or lack of knowledge and awareness about oral health in a specific demographic category. Length of diabetes information collected was combined with other measures such as awareness of the link between oral health and diabetes to learn if diabetics were taking a proactive or reactive approach towards oral health as a function of how long they have been with the disease.

Symptomatic Measures

Some of the milder oral diseases associated with diabetes discussed previously, were indirectly detected through various symptoms experienced by patients. Symptomatic measures of periodontics, salivary and neural were measured through yes or no type questions. Some example questions were: does your gums swell often, do you have dry mouth, do you have loose teeth, do you have pain in your gums or teeth, do you feel any taste alterations etc. Measuring these symptoms would inform the frequency of various symptoms experienced by diabetics.

Attitude Measures

This was one of the most important measures of this study that will help in understanding whether the diabetics have a positive or negative attitude towards oral health and their willingness to take necessary actions. Also, this measure will guide the level of intervention needed among this population. Majority of the questions related to symptomatic measures in the survey will have some relationship to attitude measures. For example, if participants responded “Yes” to gum swelling, dry mouth and pain in the gums and “Yes” to willingness to take actions, then it can be inferred that the participants have a positive attitude towards oral health.

Oral Hygiene Practices and Awareness Measures

Different oral hygiene practices measured in the study were frequency of brushing, type of tooth brush used, flossing practices, mouth wash use and frequency of dental visits. These measures would tell how knowledgeable diabetics are about oral health. One of the questions in the questionnaire measured the awareness level of oral health complications associated with diabetes among the participants. This was a yes or no type question i.e. do you know that diabetes causes oral disease.

Methods

After getting permission from the key officials at the Y to solicit participants, date and time for administering the survey was conveniently set to align with any informational session or diabetics prevention classes planned at the Y. On the set date and time, the consent form was first signed by the participants followed by filling out the questionnaire in paper format. The principal investigator was available in-person at the site to clarify any questions that might come up. Response time to the questionnaire was expected to be roughly ten minutes, but no time limit was set i.e. the participants were given as much as time they needed. The filled-out questionnaire was collected by the principal investigator on the same day. This process was repeated until 37 responses (sample size is 30) were collected. All responses were then carefully reviewed based on inclusion and exclusion criteria which would eliminate the outliers. All 37 responses were then meticulously entered in Microsoft Excel for data analysis.

Data Analysis

A collection of various descriptive analysis of different measures was used to conclude the level of awareness and knowledge of oral health among diabetics. Demographic analysis on the participants such as average age, distribution of race and sex, average educational level and mode of duration of diabetes were summarized. In addition, percentage of participants aware of and knowledgeable of various oral health habits and the association between oral diseases and diabetes were also analyzed and summarized. From awareness analysis, the study evaluated the relationship between length of diabetes and awareness among survey participants. For example, the number of “Yes” responses for awareness question was computed for each duration of diabetes category to understand the relationship between length of diabetes and awareness among survey participants. Similarly, number of symptomatic measures experienced by the participants was also computed. The oral health awareness measure was analyzed in relation to education level and family income. Finally, a correlation analysis between symptomatic and hygiene measures were tested to know whether better habits helped with lesser symptomatic measures and alternatively if poorer habits make symptoms worse.

All these analyses are expected to guide the future research in reactive versus proactive approach to oral health for diabetics. If participants wait for symptoms to get worse (i.e. having more symptoms) to be willing to take actions then it is a reactive approach. This could possibly indicate that the future interventions should focus on basic awareness about the causal relationship between oral health and diabetes. On the other hand, if the analysis concludes that the participants are generally proactive (i.e. having less symptoms and willing to take actions), and then the future interventions could focus on ways to reinforce knowledge, awareness and or the attitude.

Results

A total of 37 participants responded to the survey questionnaire. Of the 37 responses received, 7 responses were in valid as participants did not meet the inclusion criteria (4 non-diabetics, 2 were from medical profession and 1 had denture) and the remaining 30 responses were included in the analysis. The average age of the participants was 68.97 years with a standard deviation of 7.97. The demographic information of the participants (n=30) is described in Table 1. The proportion of male and female participation was approximately equal at 53% and 47% respectively. Similar trend was seen in the family income category with 43% of respondents earning below \$50K and 57% earning above \$50K. Respondents with greater than 2 years of diabetes constituted 77% which was the largest group followed by 13% with 1-2 years and 10% with less than 1 year. All 30 respondents were whites and had at least a high school level of education.

Table 1: Summary of Demographic Information of Survey Respondents (n=30)

Demographic variables	count (n)	percentage (%)
Sex		
Male	16	53%
Female	14	47%
Race		
White	30	100%
African American	0	0%
Hispanic	0	0%
Asian	0	0%
Other	0	0%
Education		
No formal education	0	0%
High School	10	33%
College Degree or greater	20	67%
Family Income		
Below \$50k	13	43%
Above \$50k	17	57%
Duration of diabetes		
Less than 1 year	3	10%
1-2 years	4	13%
Greater than 2 years	23	77%

Awareness Measures

Overall, 67% of respondents were aware of the link between diabetes and oral health and a good 33% were unaware as illustrated in Figure 5-A. The awareness level was measured as a function of three

variables namely; length of diabetes (Figure 5-B), education level (Figure 5-C) and income level (Figure 5-D). 71% of the respondents with less than 2 years of diabetes were not aware of the link, while only 22% of the respondents with greater than 2 years of diabetes were unaware. 40% of respondents with a high school level education compared to 30% of respondents with a college degree or greater were unaware of the link. Interestingly, more respondents with income level of below \$50K (77%) were aware of the link as opposed to respondents with income level of above \$50K (59%).

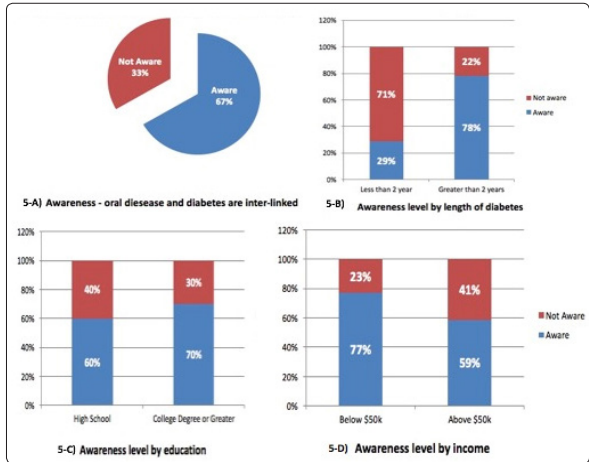


Figure 5: Graphical representation of survey data of awareness of link between oral health and diabetes and socio-economic measures

Figure 5-A: Overall awareness link among all respondents (n=30)

Figure 5-B: Awareness link based on length of diabetes (less than 2 years and greater 2 years)

Figure 5-C: Awareness link based on education level (High school and college or greater)

Figure 5-D: Awareness link based on income status (less than \$50K and greater than \$50K)

Attitude Measures

Respondents were asked 6 oral symptomatic questions and their willingness to act towards addressing those symptoms. In general, a clear majority (87%) was willing to act irrespective of the gender (male 88%, Female 86%) as shown in Table 2.

Table 2: Cross Tabulation of Attitude Measure – Willingness to Act in-case of Oral Symptoms among Survey Respondents (n=30)

n=30	Willing	Not Willing	Total
Male	14 88%	2 13%	16 53%
Female	12 86%	2 14%	14 47%
Total	26 87%	4 13%	30 100%

Oral Symptoms Measures

A total of six oral symptoms were measured namely, ulcer or burning sensation in mouth, taste alterations, dry mouth, swollen gums, pain in gums or teeth and bad breath. As shown in Figure 6, the top three symptoms experienced among respondents were dry mouth, taste alterations and pain in gums or teeth with a prevalence of 27%, 17% and 17% respectively. Ulcer or burning sensation in mouth (7%), swollen gums (10%) and bad breath (7%) were the less prevalent symptoms in this study group.

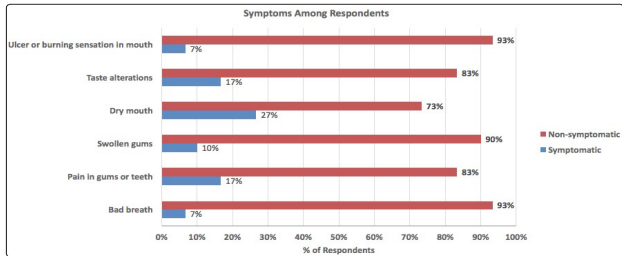


Figure 6: Oral Symptoms Measures Experienced by Survey Respondents, Diabetics (n=30)

Oral Hygiene Practice Measures

Brushing at least once a day and everyday practice of flossing and use of mouth wash were the three oral hygiene practices measured to study the level of oral health knowledge among the respondents. As depicted in Figure 7, 73% of the respondents did not follow the all three hygiene practices which leave only 27% conforming to dentists recommended everyday oral hygiene practices.

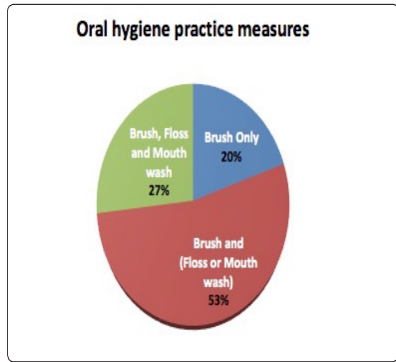


Figure 7: Daily Recommended Oral Hygiene Practice Measures followed by Survey Respondents (n=30)

Relationship of Oral Hygiene Practice and Oral Symptoms Measures

All possible combinations of oral hygiene practices (brushing, flossing, mouthwash use and regular dental visits) and symptoms measures (gingival swelling, dry mouth, bad breath and burning sensation) were plotted to analyze the co-relationship between the two. As illustrated in Figure 8, a plot of 840 data points revealed a positive linear relationship with an R-squared value of 0.67 (R=0.82) between oral habit score and symptomatic score i.e. more habits the respondents had, the less symptoms they experienced.

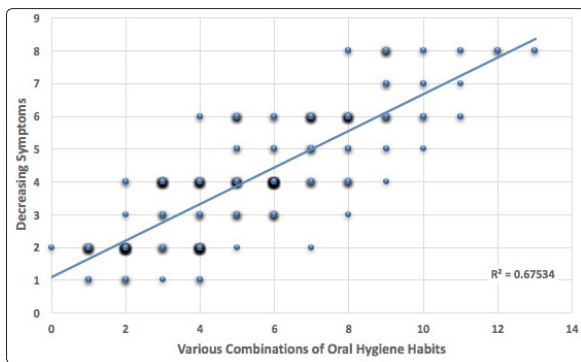


Figure 8: Correlation Plot of All Combinations of Oral Hygiene Habits and Decreasing Number of Symptoms. Oral Hygiene Habits Analyzed is Brushing, Flossing, Mouthwash Use and Regular Dental Visits. Symptoms Measures Analyzed is Gingival Swelling, Dry Mouth, Bad Breath and Burning Sensation

Dental Visits

Out of 30 respondents, 22 (73%) of them visit dentist at least once every 6 months with one of the respondents visiting dentist once every 4 months.

Discussion

This study analyzed the current oral health awareness, knowledge and attitude among diabetics as there is ample evidence to prove the strong association between oral health and diabetes which puts diabetics more at risk of being susceptible to oral diseases. This unique and very specific study is one of the very few conducted on this topic which is why connections to previous research could not be made. However, this could be the genesis of future investigations and development of intervention programs which is discussed later in this section.

The descriptive statistical analysis of the demographic variables of the study population (n=30) showed the homogenous nature of the participants; mean age of 68.97 (SD 7.97), over 75% having diabetes for greater than 2 years, 100% with education level of at least high school and 100% whites. In addition, gender and income level were equally represented at an approximately even split. As a result, data outliers were minimal and the results of this study can be generalized to specific demographics as described above but not to overall diabetic population.

The penetration of awareness of the link between oral health and diabetes among this study group was above average but not adequate as 33% of respondents did not know the link existed. As expected, slightly higher percentage of people with college degree was aware of the link. In contrast to the widely-accepted thought, 41% of respondents earning above \$50K were unaware of the link compared to only 23% with income level of \$50k and below. As explaining this difference is beyond the scope of this study, further research is needed to investigate this anomaly. Interestingly, there is a significant difference in the awareness of link between oral health and diabetes and length of diabetes. Among respondents with less than 2 years of diabetes, only 29% were aware compared to 78% of the respondents with greater than 2 years of diabetes. This shows that as the length of diabetes increases, the number of people becoming aware of the link also increases. The reason could be as the length of diabetes increases, the symptoms might be more prevalent causing

respondents to visit dentist and/or physician office where they might learn the link. This elicits the reactive behavior among diabetics towards their oral health. The attitude measure of willingness to act was exceptionally high among this group, which means an intervention program about oral health would be well received. Over 73% of this group is disciplined about visiting a dentist at least once every 6 months which is recommended by American Dental Association (ADA). With respect to oral symptoms measures, majority of respondents (at least 70%) were asymptomatic. The rationale could be that this group of respondents had a good control over their diabetic level and visit dentists regularly. With above average awareness, less symptoms, exceptionally high willingness to act and good practice of regularly visiting dentist, one might expect good oral habits amongst this group. However, the results revealed that only one fourth of this group followed all three everyday oral hygiene habits of brushing at least once a day, flossing and using mouth wash. Even more concerning is the fact that one fifth of the group followed only one oral hygiene habit i.e. brushing. Despite poor oral habits, majority of diabetics in this group had fewer oral symptoms, the reason for which could be visiting dentist regularly.

In order to find if following more habits had a positive impact on controlling the symptoms, a correlation analysis was done on all combinations of four habits and all combinations of 4 oral symptoms. With a correlation coefficient r value of 0.82, it can be inferred that, the more oral hygiene habits diabetics follow, the less symptomatic they are. In short, a combination of visiting dentists regularly and following all three everyday oral habits could alleviate most if not all symptoms leading to high quality of oral health. This means, a behavior change among diabetics from a reactive approach to oral health to more of a proactive approach is required.

Future Implication and Application

There are two crucial implications of this study, one being creating an “awareness for awareness” campaign among physicians and two, reinforcing diabetic intervention programs with oral health component. Diabetics should be made aware of the link between oral health and diabetes during the pre-diabetic stage or within the first few weeks of physician’s visits. This involves physician’s office giving clear instructions on the link between diabetes and oral health during initial visits after the diagnosis of diabetes instead of waiting for the oral symptoms to appear. Second, diabetics intervention programs focus on life style changes such as daily exercise, diabetic friendly culinary lessons etc. but oral health component involving oral hygiene practices is not covered. This study recommends including oral health modules in the diabetic intervention programs. So, either one of these approaches or in combination would enable proactive approach of diabetics towards oral health.

Limitations of the Study

The three major factors contributing to the weakness of this study are choice of sampling method i.e. convenience versus random sampling, very limited number of previously published scholarly articles on this subject and much smaller percentage of people with type 1 diabetes. A detail elaboration of these major weaknesses is listed below.

1. All respondents are whites so the awareness and knowledge level among minority or vulnerable population could not be analyzed.
2. All respondents are elderly and the mean age is 68. So, this study was not able to find whether some of the oral symptoms

were due to aging or diabetes. The results of this study could not be applied for youngsters.

3. All respondents live in the state of Massachusetts which is known as healthiest state in the U.S (United Health Organization, 2018). This could be the reason for visiting dentist regularly, having positive attitude towards oral health and high level of awareness.
4. Minimum sample size was chosen for convenience but larger sample with random sampling is needed to improve validity of the results.
5. All respondents had at least high school level of education so they might have known the importance of oral health which could have skewed the measure of awareness level.
6. This study results could not be compared with previous literature as there was not many similar studies done in the past.
7. All respondents were diagnosed with type 2 diabetes so type 1 diabetics were not represented.

Despite the above limitations, the fact that this is one of the first few studies conducted about this topic, could be the genesis of future investigations and development of intervention programs. In addition, albeit the study results could not be generalized for wider population group, this study might be valid for this homogenous demographic group.

Conclusion

This study was undertaken to analyze the oral health knowledge, awareness and attitude among diabetics with a potential future application of improving intervention programs specifically designed for diabetic people. The results of this study accomplished the original intent with some interesting findings. Although this specific diabetic group consisted of characteristics that favor oral health behaviors such as a positive attitude towards oral health and above average awareness of the link between oral health and diabetes, that did not translate to good oral hygiene practices on a day to day basis. This study further analyzed if having good oral hygiene practices converted to better oral symptoms management. A correlation analysis between these two led to conclude that there in fact is a strong positive relationship between the two i.e. higher the number of oral hygiene practices followed, the lesser the number of symptoms experienced. Thus, reinforcing the practices of oral hygiene through diabetic intervention programs could improve the overall quality of life for diabetics [15].

References

1. World Health Organization (2017) Diabetes. Retrieved from Media Center: <http://www.who.int/mediacentre/factsheets/fs312/en/>.
2. American Dental Association (2017) Diabetes. Retrieved from Oral Health Topics: <http://www.ada.org/en/member-center/oral-health-topics/diabetes>.
3. CDC (2016) Diabetes. Retrieved from Chronic Disease Prevention and Health Promotion: <https://www.cdc.gov/chronicdisease/resources/publications/aag/diabetes.htm>.
4. American Diabetes Association (2017) Overall Numbers, Diabetes and Prediabetes. Retrieved from Statistics about Diabetes: <http://www.diabetes.org/diabetes-basics/statistics>.
5. CDC (2016) Oral Health United States. National Center for Health Statistics. US Government Printing Office.
6. Colin D Mathers, Dejan Loncar (2006) Projections of Global Mortality and Burden of Disease from 2002 to 2030. Public

Library of Science (PLOS).

7. National Institute of Health. (n.d.). Health Statistics. National Institute of Diabetes and Digestive and Kidney Diseases, U.S Department of Health and Human Services. Bethesda, MD: The National Institute of Diabetes and Digestive and Kidney Diseases Health Information Center.
8. ASMBS (2013) American Society for Metabolic and Bariatric Surgery. Retrieved from Type 2 Diabetes and Obesity: Twin Epidemics: <https://asmbs.org/resources/weight-and-type-2-diabetes-after-bariatric-surgery-fact-sheet>.
9. American Dental Association (2015). Oral Health and Well-Being in the United States. Health Policy institute.
10. ODPHP (2017) Office of Disease Prevention and Health Promotion. Retrieved from Healthy People 2020: <https://www.healthypeople.gov/2020/topics-objectives/topic/oral-health>.
11. Surgeon General's Report (2014). Oral Health in America: A Report of the Surgeon General - Executive Summary. National Institute of Health, National Institute of Dental and Craniofacial Research. Rockville, MD: US Department of Health and Human Services.
12. Morbidity and Mortality Weekly Report (MMWR) (2005). Dental Visits Among Dentate Adults with Diabetes: United States, 1999 and 2004. Center for Disease Control and Prevention. Washington DC: U.S. Government Printing Office.
13. Strauss SM, Singh G, Tuthill J, Brodsky A, Rosedale M, et al. (2013) Diabetes-related knowledge and sources of information among periodontal patients: is there a role for dental hygienists? *J Dent Hyg* 87: 82-89.
14. Allen E, Ziada H, O'Halloran D, Clerehugh V, Allen P (2008) Attitudes, awareness and oral health-related quality of life in patients with diabetes. *Journal of Oral Rehabilitation*.
15. United Health Organization (2018). America's Health Rankings-Annual Report 2017. Minnetonka, MN: United Health Foundation.

Copyright: ©2018 Manju Natarajan. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.