Review article

Journal of Oral & Dental Health

A dental hygienist's role in Pakistan: reduction of overall systemic disease

Sabrina P. Heglund* and Ali Sadiq

Diploma in Dental hygiene program, Aga Khan University, Karachi Pakistan.

***Corresponding author**
Sabrina P. Heglund, Diploma in Dental hygiene program, Aga Khan University, Stadium Road, PO Box 3500, Karachi, Pakistan, 74800, Tel: +92 21 3486 3711, Fax: +92 21 3493 4294, E-mail: sabrina.heglund@aku.edu.

Submitted: 25 Apr 2017; **Accepted**: 23 May 2017; **Published**: 27 May 2017

Abstract

Dental hygiene, as acknowledged in North America, is a relatively new idea in Pakistan. The country's statistics on diabetes, preterm low birth weight babies, oral cancers and obesity is high. Relating oral health to systemic health may facilitate the acceptance of dental hygiene as a preventive therapy for systemic diseases and also in early detection of otherwise disfiguring oral cancers. This paper intends to reconnect inflammation in the oral cavity to inflammation driven systemic diseases and outcomes in the rest of the body. Prevention of oral disease may ameliorate the initiation or perpetuation of systemic diseases or associated negative health outcomes. Dental hygienists graduating from the Diploma in Dental Hygiene Program at the Aga Khan University in Karachi, Pakistan have embarked on this journey. The Aga Khan University is an independent research university that supports student and faculty research with interdisciplinary support through strength in research and excellence in education. (https://www.aku.edu/about/at-a-glance/Pages/our-vision.aspx, accessed May 2, 2017)

Introduction

Dental hygiene, as an academic program at the Aga Khan University and Hospital in Karachi, Pakistan, is a relatively new concept. The current population of Pakistan is almost one hundred and ninety-six million, based on the latest United Nations estimates [1]. The median age of the population in Pakistan is 22.7 years. A young population growing rapidly in sheer numbers, needs consideration in terms of addressing preventable health issues. However, in Pakistan, poverty is apparent everywhere one turns [2]. Vaqar and O'Donoghue published their paper in 2010 but reported on findings from 2007-2009. Jawaid in 2014 said that patients rely on myths and roadside "medically" trained charlatans to alleviate pain and suffering [3]. From his article, it seems that corruption is at the heart of the problem.

Dental hygiene is alive and doing well in developed countries. Dentists usually recommend a visit to the dental hygienist on a regular basis. In Karachi, many UK, Canadian and US dental professionals have participated in laying the ground work for a dental hygiene program that was launched in 2014. The program is of two year's duration and awards a diploma at its completion. The Health Education Commission of Pakistan has recently granted the Aga Khan University, a two- year Associate Degree of Science in Dental Hygiene to begin in January 2018.

The focus of this paper is to reconnect oral health to improved overall health in a poverty-stricken area. Medical and dental professionals may not be able to spend time to educate the population about the simpler control of oral inflammation to prevent complicated systemic inflammatory driven issues, since they are overwhelmed by secondary and tertiary patient health needs on a daily basis. Dental hygienists could be licensed and available to attend to the educational needs and simple prevention measures (primary care) of this at-risk population to reduce further expensive medical therapy and hospital care. Therapy and hospitalization comes at great expense and poverty levels can dictate many negative outcomes.

Periodontal diseases

Periodontal disease can be separated into gingivitis, inflammation of the gingiva (gums) and periodontitis, inflammation and breakdown of the periodontal structures (bone and supporting fibers). These inflammatory diseases originate from the retention of dental plaque biofilm against the soft gingival tissues surrounding the teeth [4]. Inflammation of the gingiva leads to the activation of the immune system. In this activation of the immune system all the usual players are recruited as they are during systemic inflammation. A discussion of the inflammatory process and its key players is beyond the scope of this paper. Suffice it to say that neutrophils drawn to the site attract and deploy macrophages which release interleukin – 1 (IL -1) and tumour necrosis factor – alpha (TNF- α). C-reactive proteins (CRP) produced by the liver in cases of inflammation impairs intracellular insulin signaling [5]. Periodontitis patients have been shown to have high levels of CRP and IL-6 levels with IL-6 levels being correlated to more severe periodontitis [5]. Inflammation in the periodontium is characterized by these and further dysregulations of host derived inflammation mediators such as prostaglandins and cytokines. Cytokines, such as MMP-8 and MMP-9 (matrix metalloproteinases), T cell regulatory cytokines, and chemokines have been intensively studied for their roles in inflammation [5].

Periodontal disease such as gingivitis can be reversed with regular simple home based tooth brushing and flossing to remove dental plaque biofilm at the interface of the gingiva and tooth. However, disease reversal is not possible in periodontitis. Here the alveolar bone loss cannot be regenerated with simple home and professional preventive treatments like tooth brushing, flossing and professional periodontal debridement of calculus from tooth surfaces. However, the non- surgical periodontal therapy (NSPT) technique may be employed to arrest the disease and to prevent further destruction. Regularly scheduled periodontal maintenance assists in retaining better periodontal health by disturbing the environment surrounding the tooth itself thus preventing microbial colonization. Essentially, simple tooth cleaning by the patient in a habitual and efficient manner can protect the oral tissues from inflammation. The reduction of inflammatory immune proteins coursing through the bloodstream will aid in reducing the inflammatory effects on other organs and systems.

Diabetes

Diabetes is an enormous problem in Pakistan and in many low socioeconomic communities in developed countries [4]. Diabetes runs in families and can be classified as a genetically inherited disease. There are tremendous costs associated with maintaining diabetic patients in a balancing act of health. Dental hygiene students also see patients who refuse to take the medications due to the high cost of pharmaceutical drugs. During interdisciplinary course work these students see a great deal of poverty first hand as they visit slums to provide outreach education, such as tooth brushing techniques, and participate in research carried out by students from Community Health Sciences. With inadequate access to care and medications, blood sugars careen out of control and the patient, as well as the medical provider cannot get a handle on it. Outcomes are not favourable when these sugars fluctuate to dangerously low or high levels. Emergency rooms have many such patients presenting for treatment who may not even know they are diabetic. Costs for even one ER visit are astounding. In developed countries too, this problem is still present. It places a huge burden on government subsidized health care plans where they are available. However, there are no health care plans in Pakistan.

The mere presence of diabetes in a periodontally involved patient raises the risk of losing more teeth and having more infections in addition to the patient's reduced general healing potential. Preshaw et al reviewed the literature and noted that there is a clear relationship between the degree of hyperglycemia and severity of periodontitis [6]. Data from the World Health Organization (2011) stated that the prevalence of diabetes in Pakistan is 12.9 million people (10% of the total population) [7]. Of those there are 9.4 million diagnosed cases and 3.5 million undiagnosed cases. With 38 million people existing with pre-diabetes, 20.5 % are women and 15.9% are men. It is estimated that Pakistan has become the seventh largest country in terms of diabetes for the population and it will be fourth largest by the year 2030. This is an alarming figure and shows a bleak outlook for the people of Pakistan.

Inflammation has long been linked to control of sugars in diabetics. It was noted in Preshaw et al, (2012) that reduction in probing pocket depths in a type I diabetic resulted in reasonably better Hb A1C levels [5]. People presenting with periodontitis do not necessarily have any associated pain. The disease becomes problematic when teeth become mobile. Gingivitis although painless makes more of an impact because of bleeding that occurs in conjunction with eating or brushing. Advertising by pharmaceutical companies on the merits of toothpaste to reduce gingivitis are prolific. What may not be easily comprehended is that it is the mechanical action of brushing that is needed to physically remove dental plaque biofilm at the gingival margin. What gets highly promoted is the application of toothpaste in large amounts delivered via a toothbrush as being responsible for the dramatic healing. There is a disconnection that needs to be openly discussed at a level that poverty-stricken people can understand. In Pakistan, as in some other developing countries, the use of miswak sticks to cleanse the oral cavity has been going on for thousands of years. People who cannot afford toothbrushes or toothpaste can be educated in the use of miswak for the effective removal of dental plaque biofilm at the gingival margin.

Preshaw et al stated that the importance of diabetes as a major risk factor for periodontitis became evident in the study of the Pima Indian people in the 1990's [5]. Preshaw et al, called periodontitis and diabetes a two-way relationship [5]. Although the links between the two have not been understood completely, aspects of neutrophil activity and cytokine signalling due to enhanced immune functioning are involved. Macroalbuminuria and end stage renal disease (ESRD) show two-fold and three-fold increases in patients with both diabetes and periodontitis. The levels of systemic markers of inflammation are elevated in both type I and type II diabetes which contributes to microvascular and macrovascular complications [8]. It is known that hyperglycemia can activate pathways to increase inflammation and oxidative stress. Elevated levels of IL-6 and TNF-α are seen in diabetes and obesity while CRP and IL-6 levels may predict the occurrence of type II diabetes and more severe periodontal breakdown. The prostaglandin, PGE2 levels found in gingival crevicular fluid, (fluid exudate in the gingival margins which has a higher flow rate in disease) were higher in patients with type I diabetes presenting with simple gingivitis or more severe periodontitis when compared to non-diabetic patients with equivalent levels of disease.

A dental hygiene diagnosis of periodontitis with xerostomia and candida infections may be a sign of possible diabetes in the patient. By bringing the finding forward to the dentist during the dental examination, the hygienist has done due duty and the dentist may suggest the patient visit the physician for tests for diabetes. It is in the detection of oral conditions that may not initially bring the patient into the dental office, but being found in a routine dental hygiene appointment that may contribute to the overall systemic well-being of the patient in a more cost-effective manner.

Preterm low birth weight babies

Pakistan, a developing country, has a high rate of pre-term low birth weight babies (PTLBW) [9, 10]. In PTLBW babies, the financial burden applies long after the infant is released from the NICU or ICU. These children suffer multiple afflictions ranging from respiratory problems to reduced mental functioning. The costs of care for one premature baby throughout his/her lifetime become a formidable burden.

Since 1990, PTLBW babies were prominent in the dental scientific journals. Upon closer study, porphyromonas gingivalis, tannerella forsythia, campylobacter rectus, fusobacterium nucleatum were some of the oral microorganisms found in amniotic fluids [11]. Cytokines produced in the presence of periodontal inflammation are easily taken up into systemic circulation via severely inflamed gingival tissue that becomes more porous. Pro-inflammatory cytokines stimulate the production of prostaglandins that can increase contractility of the uterine walls thus promoting premature birth [12]. Preterm birth is a delivery at less than 37 weeks of pregnancy and accounts for a large percentage of perinatal mortality and long-term morbidity [13].

Perinatal mortality and complications from PTLBW babies are quite high in Pakistan. It is almost 10 times higher than in developed countries [14]. A fact sheet issued by the World Health Organization (WHO) suggests that Pakistan is one of 10 countries with highest incidence of preterm birth. Of every 100 live births in Pakistan, 15.8 babies were born before 37 weeks of pregnancy [15].

Babies born prematurely could suffer from cognitive disorders and impeded physical growth [15]. Prematurity is a leading cause of death in children under 5 years of age [16]. Overall, the rate of child deaths in the world is declining. However, the child death rate related to preterm birth is not declining at the same pace. There are many reasons for that - one being that preventive interventions are not provided in a timely manner to vulnerable women.

Periodontitis as a chronic, low grade, plaque induced immune response, manifests as an inflammatory condition. Researchers have studied the evidence suggesting an association between periodontal inflammation and systemic conditions. These studies have found associations at varying rates [17]. Several studies that controlled for common confounders, have reported the odds ratio (OR) between 3.5-7.9. The mechanism behind this association is not fully understood. However, some evidence proposed infection-induced parturition as a biologically plausible mechanism behind the link between periodontitis and preterm birth [18]. The role of intra-uterine infection (IUI) and preterm birth are well documented but the question remains as to how the infection of a distant arena such as periodontal tissue could have the same affect or at least be a risk factor [19]. Intra-uterine infections increase the production of local cytokines such as interleukin-1 (IL-1) and tumour necrosis factor alpha (TNF α) which are also elevated in periodontitis. These markers may be transported to the target site through the blood and may potentially cause the same effect as locally produced cytokines. Therefore, elevated levels of cytokines seen in periodontitis may be one reason behind the association between periodontitis and preterm birth [20]. A prospective study further strengthened the association by suggesting a dose-response relation between severity of periodontitis and decreasing gestational age at birth [18]. Finally, early findings from intervention studies indicate that periodontal therapy during pregnancy may result in a reduction in the incidence of PTLBW babies [20]. Root surface debridement (scaling) is one cost effective and time proven treatment modality to manage chronic periodontitis. A meta-analysis of randomised controlled trials has shown a reduction in the incidence of preterm birth and low birth weight in women who receive periodontal therapy during pregnancy [21, 22].

The health care infrastructure in Pakistan is built in a way that more resources are invested in tertiary health care, requiring more financial output, with fewer people getting benefit from it. Whereas, if more was invested in primary care services and preventive measures such as improving oral hygiene, larger populations may be targeted with much less resource expenditure. An example of primary preventive care at a government level is water fluoridation which has been shown to be a successful caries preventive measure at the community level [23].

At this point we lack large randomised control trials to conclusively state that periodontitis is a true risk factor for perinatal complications. However, let one consider that periodontal therapy does no harm to a pregnant woman or her fetus and it also has the probability of reducing perinatal complications. Healthcare professionals should be very cautious before rejecting treatment of periodontal disease with scaling and/or root planning before or during pregnancy. Preterm birth related mortality has a high financial burden requiring sophisticated intensive care units to manage premature babies. This is reflected in the survival rate disparity of premature babies in high-income countries versus low-income countries. Babies born less than 28 weeks gestationally, have a 90% survival in high-income countries whereas that value stands at 10% in low-income countries such as Pakistan [14]. The lack of resources, high burden to health care and the state of the welfare system in countries like Pakistan highlights the need to invest more in evidence-based clinical and population-based interventions that can reduce the risk of PTLBW babies.

It may be said that oral hygiene education, if not periodontal therapy itself, should be discussed with pregnant women. If one considers periodontitis being a potential risk factor and that it has an overall effect on PTLBW babies, an argument can be made that dental hygiene therapy increases a patient's oral health related quality of life. In this regard, the dental hygienist could play an important role in allied health care to implement these cost effective preventive interventions at a community level. This may lead to full term babies born to periodontally healthy mothers who just by kissing their babies have the potential to transmit bacteria that could lead to their child being more at risk for cavities and periodontal disease.

Oral Cancer

Pakistan as a developing country has one of the highest rates of betel chewing. Khan, Bawany, and Shah stated that "A study conducted in a Karachi squatter settlement showed that 40 per cent of the population was involved in chewing of betel nuts and tobacco on a regular basis. It's likely that betel nut is the second most common consumed carcinogen after tobacco in the subcontinent" [24]. In the dental clinic in Karachi, many occurrences of oral cancers have been reported. The disfiguring surgeries are apparent in those patients (men and women) attending oncology support groups wearing medical face masks covering their lower face. WHO noted the rate of oral cancer in Pakistanis is higher than in other countries and is more prevalent among certain communities [25]. Dental hygiene students are taught early in the first semester of their study, the method of conducting an oral cancer scan. At that point, they are still not familiar with head and neck anatomy, but are told to practice the technique on every patient until they later learn the names of the areas they palpate.

A dental hygiene oral cancer scan can take early learners about five minutes, but once competency is gained, it takes about a minute. That is a small price of time to pay for early detection of oral cancers. The students practice these techniques at the school and go out to the poorer quarters once a week to carry out scans and teach mouth care. This is done at a basic level, and suggestions are made to see a dentist or a physician, though there is little hope for the people in these areas to afford a dental check-up, or a doctor's visit. On the other hand, the mere presence of dental hygienists carrying out education may assist the families in becoming aware of the hazards. Reduction in use of these carcinogenic substances may be a desired outcome. Dental hygienists in Pakistan would be able to carry out inspections such as these with very few supplies. Dental hygiene being a new profession needs licensing by the government or dental body to work in remote areas and in the slums of Pakistan.

The incidence of oral squamous cell carcinoma (SCC) remains high in India and Pakistan. In Karachi, during the last few years, it is being diagnosed in younger people [26]. In one of the studies, the youngest patients were twelve years old. Tobacco is used as a hunger suppressant in most cases. It is cheaper to purchase a single cigarette for Rs. 2.00 than a chappati (local bread) for Rs. 10.00. In visits to some of the poor quarters with students from the program, it was found that even four and five year old children have a packet of gutka (tobacco related chewing product) in their pockets. One survey in Karachi indicated that 36% of the males and 44% females chew paan (betel nut) with tobacco [27]. In the Pakistani culture, women are never seen smoking cigarettes, but still have high incidences of SCC. In Pakistan the male to female ratio was 1.5:1 for head and neck cancers [26].

In developed countries, dental hygienists are made aware that a SCC scan should be diligent especially for the lateral borders of the tongue and the floor of the mouth. In Karachi, because of the nature of the product, cancers are often found on the buccal mucosa which may show up at first as diffuse linea alba or leukoplakia that cannot be wiped off. Half of the cases in the Alamgir et al study were under the age of 45 [26]. This study discussed the staging of SCC with needed surgery as being less complicated the earlier it is diagnosed. Observant tissue scans by a dental hygiene healthcare professional may alleviate the harshness of primary resection and reconstruction.

Oral cavity cancers are thought to be about 5% of all malignant tumors in humans [28, 29]. As Bhurgi Y, et al reported, the annual incidence rate of oral cancers is 4.1 per 100,000/year in males and 4 per 100,000/year in females [27]. Oral cavity cancers can involve the tongue, alveolus (teeth supporting dental bone), the floor of the mouth, lips, palate and buccal mucosa with buccal mucosa being suspect much more in Karachi. Oral cancers involving the head and neck are highly preventable and can be cured if they are managed well with early detection by a healthcare professional.

Self-cancer checks have not been studied to any great extent in Karachi. Most of the patients entering for dental hygiene therapy usually do not even consider a partial opening of the mouth a problem until they cannot eat anymore. Oral submucous fibrosis was present in a patient whose chief complaint was that he could not open any wider for the oral cancer scan that the dental hygienist was trying to conduct. Dental hygienists armed with education on the probable locations for early detection would benefit the rate at which disfiguring head and neck resections are carried out.

Obesity

The deposits of excessive fat in adipose tissues of humans can be called human obesity. It is increasing throughout the world and is becoming a health problem in both developed and developing countries. In a 2006 study, the prevalence of overweight persons and obesity in the general Pakistani population, was 25% and 10% respectively [30]. Boesing et al (2008) summarised obesity consequences to go further than just "adverse metabolic effects on health" They noted that there were negative effects in relation to periodontitis because of the increase in pro-inflammatory cytokines and oxidative stress [31].

The inflammatory response in obesity is characterised by increased levels of the pro-inflammatory cytokines such as IL-6 and tumour necrosis factor alpha (TNF-α). IL-6 is also associated with an increase in C-reactive proteins. Additionally, the number of leukocytes are increased in obese patients as recorded by Kullo et al (2002), along with the secretions of myeloperoxidase secreted by them which is a marker of the inflammatory response [32].

A systematic review carried out in 2010 showed a positive association between obesity and periodontitis, although it was said to have been based on data from study designs from the lower hierarchy of evidence [33]. Obesity has been thought to modulate host immune responses with an increased susceptibility to infections and exaggerated responses to them [34]. The cytokines released in inflammation are closely associated with periodontitis. In some studies, obese people were found to have altered periodontal microflora along with an increased response to them [34]. TNF-α has been shown as one of the cytokines secreted by adipose tissue and is also thought to be responsible for injury in periodontal tissue [35]. Concentrations of this cytokine was higher in periodontitis patients than in periodontally healthy patients and were reduced post periodontal therapy [35]. In obese patients without periodontitis, there was still a positive association of TNF-α from gingival crevicular and those patients' body mass index (BMI) [36].

There have been many associations made between different diseases and periodontitis. Some of the claims have been rather strongly supported and some have been refuted. However, all the claims made for associations have brought the host inflammatory response and its related cytokines and chemical messengers into the discussions around periodontal disease. Although none of the studies read to date can demonstrate a cause and effect, suggestions are made for more stringent definitions of periodontal disease or for further robust studies of large populations, with randomised samples and controls. Human research is a difficult task. The studies cannot take every suggestion under consideration, and when they do control for certain aspects, more questions than answers are generated. Inflammation brings myriad host immune reactions. Periodontitis is an immune reaction to dental plaque biofilm at the gingival margin with associated inflammation and breakdown effects. It is reasonable to suggest in the name of reducing the overall systemic disease burden in a developing country like Pakistan, prevention of the kind delivered by dental

hygiene professionals can only serve to reduce disease and promote systemic health.

Dental hygiene therapy applied by an educated dental hygiene practitioner may alleviate the financial burdens of other expensive treatments of complications. It is relatively easy to request that a patient see a dental hygienist when they present for their medical appointment. Pregnant women or those planning a pregnancy should be encouraged to go for dental hygiene therapy. Diabetics who return to medical practices time and time again with all sorts of complications may need a prescription for a dental hygiene treatment.

Children born prematurely continue to display cognitive disorders and physical growth impediments not seen in full term babies. Full term babies do not mature to adulthood needing extensive health care that can burden families and the welfare system in general. Allied health care professionals should aim for birthing of full term babies. Indeed, this may be impossible for all pregnant mothers, but easing the birth of even a few preterm babies may alleviate health problems and costs of related care.

References

1. http://www.worldometers.info/world-population/pakistan-population/.
2. Vaqar AO, Donoghue C (2010) International Journal of Micro simulation Global Economic Crisis and Poverty in Pakistan 3: 127-129.
3. Jawaid SA (2014) Standard of general practice and elimination of quackery. Pulse International 15: 6.
4. Lalia E, Papapanou PN (2011) Diabetes mellitus and periodontitis: a tale of two common interrelated disease. Nat. Rev. Endocrinol 7: 738-748.
5. Preshaw PM, Alba AL, Herrera D, Jepsen S, Konstantinidis A, et al. (2012) Periodontitis and diabetes: a two way relationship. Diabetologia 55: 21-31.
6. http://www.who.int/diabetes/publications/en/.
7. http://diabetespakistan.com/treatment/2013/05/08/diabetes-statistics-in-pakistan/.
8. Dandona P, Aljada A, Bandyopadhyay A (2005) Inflammation: the link between insulin resistance, obesity and diabetes. Trends Immunol 25: 4-7.
9. Goldenberg RL, Jobe AH (2001) Prospects for research in reproductive health and birth outcomes. JAMA 285: 633-639.
10. Mobeen N, Jehan I, Banday N, Moore J, McClure EM, et al. (2008) Periodontal disease and adverse birth outcomes: a study from Pakistan. Am J Obstet Gynecol 198: 514-514.
11. Jarjoura K, Devine P, Perez-Delboy A, Herrera-Abreu M, D'Alton M, et al. (2005) Markers of periodontal infection and preterm birth. Am J Obstet Gynecol 192: 513-519.
12. Geisinger ML (2016) Healthy mouth, healthy mom, healthy baby: Optimal oral health care before, during and after pregnancy. Continuing education Course, Dentalcare.com.
13. McCormick MC, Shapiro S, Starfield BH (1985) The regionalization of perinatal services. Summary of the evaluation of a national demonstration program. JAMA 253: 799-804.
14. Hannah B, Simon C, Mikkel O, Doris C, Ann-Beth M, et al. (2012) National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: A systematic analysis and implications. Lancet [Internet] 379: 2162-2172.
15. World Health Organization (2016) Preterm birth. Media Centre 1-5.
16. Liu L, Oza S, Hogan D, Perin J, Rudan I, et al. (2015) Global, regional and national causes of child mortality in 2000-13, with projections to inform post-2015 priorities: an updated systematic analysis. Lancet 385: 430-440.
17. Offenbacher S, Katz V, Fertik G, Collins J, Boyd D, et al. (1996) Periodontal infection as a possible risk factor for preterm low birth weight. J Periodontol 67: 1103-1113.
18. Offenbacher S, Lieff S, Boggess K, Murtha A, Madianos P, et al. (2001) Maternal periodontitis and prematurity. Part I: Obstetric outcome of prematurity and growth restriction. Ann Periodontol 6: 164-174.
19. Gonçalves LF, Chaiworapongsa T, Romero R (2002) Intrauterine infection and prematurity. Ment Retard Dev Disabil Res Rev 8: 3-13.
20. Jeffcoat MK, Reddy M, Cliver S, Goldenberg RL, Hauth J (2001) Periodontal infection and preterm birth. Results of a prospective study. JADA 132: 883-889.
21. Jeffcoat MK, Hauth J, Geurs N, Reddy M, Cliver S, et al. (2003) Periodontal disease and preterm birth: results of a pilot intervention study. J Periodontol 74: 81-104.
22. Polyzos NP, Polyzos IP, Mauri D, Tzioras S, Tsappi M, et al. (2009) Effect of periodontal disease treatment during pregnancy on preterm birth incidence : a metaanalysis of randomized trials. YMOB. Mosby, Inc 200: 225-232.
23. Hu W, Walsh T, Malley OL, Je C, Macey R, et al. (2015) Water fluoridation for the prevention of dental caries (Review). The Cochrane database of systematic reviews.
24. Khan MS, Bawany FI, Shah SR, Hussain M, Nisar N, et al. (2013) Comparison of knowledge, attitude and practices of betel nut users in two socio-economic areas of Karachi. JPMA 63: 1319.
25. https://alaiwah.wordpress.com/2011/05/13/pakistan-has-one-of-the-highest-oral-cancer-rates/.
26. Alamgir M, Jamal Q, Jafarey NA, Mirza T (2013) Clinco – pathological parameters of 50 oral squamous cell carcinoma cases in Karachi Pak J of Med Dent 2: 3-8.
27. Bhurgi Y, Bhurgi A, Nishter S, Ahmed A, Usman A, et al. (2006) Pakistan – Country profile of cancer and cancer control 1995-2004. J Pak Med Assoc 3: 124-130.
28. Begum N, Naheed G, Shagufta N, Khan A (2009) Oral cavity cancers in Northwest Pakistan: a hospital based study. J of Pak Med Inst 1: 28-34.
29. Ferlay J, Pisani P, Parkin DM (2004) Globocan 2002 Cancer incidence, mortality and prevalence worldwide. IARC Cancer Base (2002 estimates) Lyon: IARC Press.
30. Jafar TH, Chaturvedi N, Pappas G (2006) Prevalence of overweight and obesity and their association with hypertension and diabetes mellitus in an Indo-Asian population. CMAJ 175: 1071-1077.
31. Boesing F, Patino JSR, da Silva VRG, Moreira EAM (2009) Obesity Reviews 10: 290-297.
32. Kullo IJ, Hensrud DD, Allison TG (2002) Comparison of numbers of circulating blood monocytes in men grouped by body mass index. Am J Cardiol 89: 1441-1443.
33. Suvan J, D'Aiuto F, Moles DR, Petrie A, Donos N (2011) Association between overweight/obesity and periodontitis in

adults. A systematic review. Obesity reviews 12: 381-404.
34. Falagas ME, Kompoti M (2006) Obesity and infection. Lancet Infect Dis 6: 438-446.
35. Nishimura F, Iwamoto Y, Mineshiba J, Shimizu A, Soga Y, et al. (2003) Periodontal disease and diabetes mellitus; the role of tumour necrosis factor-alpha in a 2-way relationship. J Periodontol 74: 97-102.
36. Lundin M, Yucel-Lindberg T, Dahllof G, Marcus C, Modeer T (2004) Correlation between TNF-alpha in gingival crevicular fluid and body mass index in obese subjects. Acta Odontol Scand 62: 273-277.