The Effect of High Cholesterol Level on Recurrence Rate of Oral Ulcer

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Abstract

Introduction: Oral ulcers are one of the most common complaints of the oral mucosa lesion. Ulcer is defined by damage or discontinuity of the epithelium and lamina propria which usually affects the non-keratinized or poorly keratinized surfaces of the oral mucosa. It is a multifactorial condition several predisposing factors have been suggested.

Objectives: The aim of this study is to determine the relationship between the increase in cholesterol level and the presence of recurrent oral ulcer.

Materials and Methods: A case control study was conducted in oral medicine clinic Kulliyyah of Dentistry International Islamic University Malaysia, Kuantan, Pahang. Convenience sampling was used to select the sample devided into 2 groups patient with recurrent oral ulcer (ROU) (male and female) and control. Patients who fulfilled the criteria were selected. Blood cholesterol and blood pressure of both groups were mesured and recorded. Data analysis was done using independent t-test by, SPSS version 20 for Windows.

Results: Cholesterol level was significantly higher in patient with recurrent oral ulcer (6.32 ± 0.45mmol) compared to control group (4.97 ± 0.28mmol) ($p<0.05$). $t(46) = 2.75$, $p = 0.008$.It is also found that the control group had statistically significantly lower S.BP (113.77 ± 2.93 mmHg) compared to the subject group (126.62 ± 3.61 mmHg), $t(46) = 2.75$, $p = 0.008$.

Conclusions: This study emphasizes that high cholesterol level is highly associated with ROU.

Keywords: Cholesterol level, Recurrent oral ulcer, Assesment

Introduction

Ulcer is defined simply as a break in the skin or mucous membrane with loss of surface tissue, disintegration and necrosis of epithelial tissue [1]. Thus we can understand oral ulcer as an ulcer which occur in oral cavity.

The recurrent oral ulcers are the most common oral mucosal lesions characterized by the repeated formation of benign and non-contagious oral lesion that can be observed by the dentists [2]. It is usually occurring on nonkeratinized or poorly keratinized surfaces of the oral mucosa such as labial and buccal mucosa, maxillary and mandibular sulcus, unattached gingiva, soft palate, floor of the mouth, and ventral surface of the tongue [3]. Oral ulcers are one of the various developing conditions within oral cavity that is associated with painful lesions, They may be fungal, bacterial, viral infection-associated or non-infection-associated conditions. The standard treatment protocol for these oral ulcers includes the elimination of etiologic factors, pain reduction, and promote normal healing [4].

They can be classified as acute or chronic according to their presentation and progression. Acute oral ulcers are be associated with conditions such as trauma, recurrent aphthous stomatitis, Behçet's disease, bacterial and viral infections, allergic reactions or adverse drug reactions. Chronic oral ulcers are associated with conditions such as oral lichen planus, pemphigus vulgaris,

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mucosal pemphigoid, lupus erythematosus, mycosis and some bacterial and parasitic diseases [5]. It also may arise or associated with any other systemic diseases such as GIT disease, anemia, connective tissue disease and HIV disease [4].

The clinical presentation of aphthous ulcers is defined by the number of recurrences and severity of disease. Clinically, the number and size of the ulcers are the two main criteria used to divide ulcers into three forms: minor, major, and herpetiform [6]. It is a multifactorial disease. According to Zuzanna et al., 2014 [7], an altered local immune response involving a cell mediated immune response and generation of T-lymphocytes, interleukins and tumor necrosis factor in addition to the trauma, allergies, endocrine alterations and dietary components are also considered to be the most common predisposing factors [8]. Thus, patient with the frequent recurrences should be screened for disease such as anemia, diabetes mellitus, vitamin deficiency, inflammatory bowel diseases, immune suppression [9].

Cholesterol is a steroid that is present in diet, but it is mainly synthesised in the liver and small intestine, cholesterol is a major component of cell membranes, and act as the substrate for the steroid hormone formation in the adrenals and the gonads [10]. It transport throughout the body with other fats by a protein forming a substance called lipoprotein. Two common lipoproteins are High Density Lipoprotein (HDL) and Low Density Lipoprotein (LDL). It has been suggested that any changes in cholesterol level lead to alteration in immune rersponse. An increase of plasma cholesterol which lead to elevation of cholesterol and lipid leading to an alteration of lymphocytes function and reduce cell mediated immune response [11].

Although the exact cause of RAU is not known, local trauma, micro- organisms, nutritional de ciencies, hormonal changes, genetics, and immunological factors have been suggested to contribute to its pathogenesis, the aim of the present study was to assess the effect of the increase in cholesterol level and blood pressure in patients with recurrent oral ulcer [12].

Literature Review

The oral cavity is the site of the body where contact with exogenous material, micro-organisms and harmful agents are more intense. The oral mucosa functions as a mechanical and immunological barrier. Protective mechanisms are noted in the form of increased capacity for epithelial regeneration and increased keratinisation. These epithelial changes are reactive and reversible but progressive loss of normal control mechanisms leads to pre-cancerous states and oral ulcers [13].

The clinical characteristics of RAU are well de ned and successful diagnosis can be made through a careful history and clinical examination [14]. It is characterized by small (usually 1-2 mm wide) painful ulcers which typically have red borders and yellow-gray centers. They occur in inner side of the lips, the tongue, the wall of the cheeks and the back and oor of the mouth [15]. Minor, major, and herpetiform are the 3 classic forms of RAU. Minor aphthous ulcers appear as recurrent, round, closely de ned, small painful ulcers with shallow necrotic centers [16], raised margins and erythematous halos in the labial, buccal and oor of the mouth mucosa. Major aphthous ulcers are similar to the minor but are larger, deeper, often scars and can last for weeks to months. Herpetiform ulcers are the least common and appear as small and numer-ous ulcers [17].

Lipids are the major cell membrane components, which are essential for various biological functions like maintaining cell integrity, cell growth, and division of normal and malignant cells. Changes in the lipid profiles have been seen in various diseased conditions including the malignant and premalignant oral lesions [18].

Level of Cholesterol in Recurrent Oral Ulcer Patients

High level of cholesterol in Recurrent Oral Ulcer Patients

Persons with oral mucosal disease were generally at old age, with higher systolic and diastolic blood pressure, and had higher levels of triglycerides, cholesterol, and more compared with those with no oral mucosal diseases [19].

In a study done to evaluate possible association between recurrent apthous ulcer and plasma lipid level. Total Cholesterol and Low Density Lipoprotein are found to be statistically significantly higher in group with recurrent oral ulcer. If gender was considered, correlation were mostly observed between minor RAUs and parameters within the female group [20].

It is also found High Density Lipoprotein Cholesterol were found significantly higher in patients with Recurrent Aphtous Ulcer in active stage [21].

### Low level of cholesterol in Recurrent Oral Ulcer Patients

Total serum cholesterol and triglycerides were found to be a little bit higher but was not statistically significant in patient with recurrent aphthous ulcer, but where HDL was found statistically significant lower in recurrent aphthous ulcer patient.

There was a slight increase in triglycerides level in patient with recurrent aphthous ulcer but decrease in total serum cholesterol compared to normal healthy person [23].

Low level of cholesterol in Oral Cancer Patients

It is found that the lipid levels were statistically significantly lowered in patients with cancer than with the normal control group [24].

Conceptual Framework
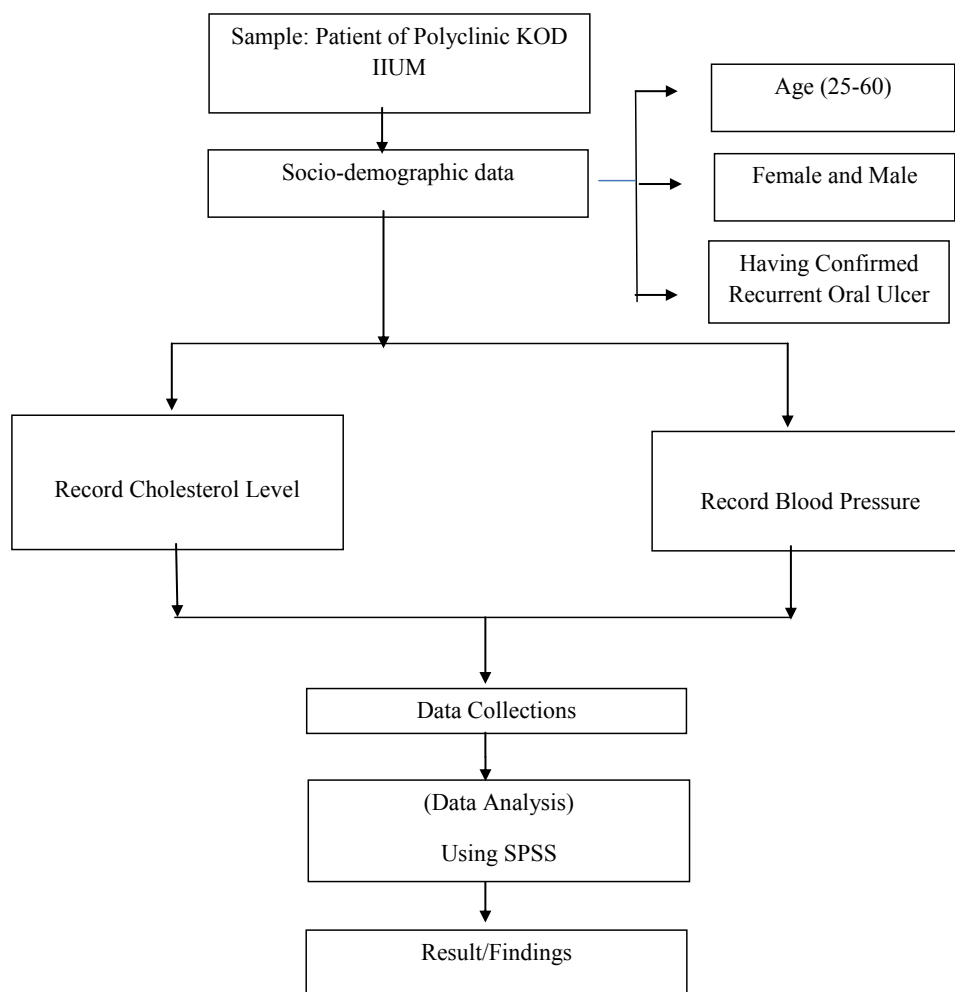
Materials And Methods

Sampling method

This study will be used the convenient sampling method. Four group will be formed in this study which involve eighty person in the range of 25-60 years old. Twenty male and female patient with recurrent oral ulcer will form two groups respectively. Another two groups will be formed by each twenty male and female healthy person without recurrent oral ulcer. As described in the above Conceptual Framework.

Sampling

Population sample: All patients in Polyclinic KOD IIUM, male and female in the range of 25-60 years old who are willing to participate in this study.

Sample size: The estimated sample size is 80, which will then be divided into four groups.

Group I :20 male with recurrent oral ulcer.

Group II :20 female with recurrent oral ulcer.

Group III :20 male without recurrent oral ulcer.

Group VI :20 female without recurrent oral ulcer.

Inclusion Criteria

Patients who is having clinically confirmed with Recurrent Oral Ulcer, adult male and female patients with age range of 25-60 year old.

Exclusion Criteria

Patients having disease that can alter the lipid profile (nephrotic disease, diabetes). Patient that taking cholesterol and lipid modifying medications (corticosteroid). Patient that taking oral contraceptive medications. Patient using tobacco related product – smoking or smokeless tobacco.

Instrument

This study will use the Oral Medicine Year 4 and Year 5 case sheet. Besides the multi parameter system meter device (Human Sens Plus) will be used in this study to analyse the cholesterol level that taken from the sample. The

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sphygmomanometer device will also be used to take the blood pressure of the sample.

Variables

Independent variables

1. Subject group with recurrent oral ulcer male and female.

2. Controlled group without recurrent oral ulcer male and female.

Ethical consideration

Ethical clearance was obtained from the ethics review committee of International Islamic University Malaysia (IIUM) (IREC), Kuliyyah of Dentistry Research Committee (KDRC). The purpose of the study and the privacy and confidentiality issue was explained to the respondents and written consent was taken. Data obtained in the research only be used for academic purpose which is for this study only. All data are confidential as no part of it will be sold to or reused by other people either a research or non-research purpose without the notification and permission of the respected respondents.

Data Collection

Data collection had taken place within January to July 2015.

The oral lesion confirmed to be recurrent oral ulcer by the authors and verified by the specialist that supervised during the time. Blood cholesterol level of the patient was taken and analysed by using multi parameter system meter device (Human Sens Plus). Patient blood pressure was measured when the patient is sitting during rest, using sphygmomanometer device. It was measured twice with interval of 5 minute between the two measurements then the average is calculated. Everything noted down on the oral medicine case sheet and the picture of the oral ulcers were taken as a proof. The case sheet paper were then put in an a confidential envelope to be used for data analysis. After one or two weeks, the patient was reviewed to observe the healing recurrent and it was confirmed by the supervisor or specialist during the time.

Data Analysis

Statistical test used

The collected data was analysed by using a computer statistical program, SPSS version 20 for Windows. Data described using means and standard error of the mean (SEM). The data was analyzed using independent t-test and one way-Anova was used for multiple comparisons to find the mean differences between the groups at different time interval. The level of statistical significance was be set at P-*value* was set at ($p < 0.05$) for all analyses.

Results

This study found that the subject group had statistically significantly higher cholesterol concentrations (6.32 ± 0.45

Table 1: Relationship between control and subject group.

Group	N	Mean	SEM	*t*	p
Control					
Age	23	36.17	1.85		
S. BP (mmHg)	24	113.77	2.93		
D. BP (mmHg)	24	81.75	2.37		
Cholestrol (mmol)	24	4.97	0.28		
Subject					
Age	24	37.58	2.65	0.432	0.668
S. blood pressure (mmHg)	24	126.62	3.61	2.758	0.008
D. blood pressure (mmHg)	24	84.87	2.62	0.479	0.381
Cholestrol (mmol)	24	6.32	0.45	2.526	0.016

mmol) compared to the control group (4.97 ± 0.28 mmol), t (38.75) = 2.52, $p = 0.016$ as seen in Table 1.

As shown in Table 1, this study found that there is no statistically significant difference in age between the control group (36.17± 1.85 years) and the subject group (37.58 ± 2.65 years), t(45) = 0.43, $p = 0.668$.

This study also found that the control group had statistically significantly lower S.BP (113.77 ± 2.93 mmHg) compared to the subject group (126.62 ± 3.61 mmHg), t(46) = 2.75, $p = 0.00$ as illustrated in Table 1.

This study found that there is no statistically significant difference in D.BP between the control group (81.75 ± 2.37 mmHg) and the subject group (84.87 ± 2.62 mmHg), t (46) = 0.47, $p = 0.884$, as referred to Table 1.

Discussion

Since the recurrent oral ulcers are the most common chronic inflammatory disease of the oral mucosal tissues characterized by the presence of single or multiple ulcers persisting and recurring for variable period of time [25].

In normal conditions, mucous membrane are protected from the damage caused by harmful molecules, as well as from the free radicals by the protective surface phenomena [26]. Many studies proved that cholesterol is a vital and essential structure for the maintenance of integrity of biological cell membranes and cellular uptake [26]. Thus it is worthy to mention that cholesterol and lipids are fundamental components for various biological functions including cell growth and division in both normal and diseased tissue (neoplastic or inflamed) [26].

For this any changes in cholesterol and lipids profile would be associated with many inflammatory and neoplastic lesions as lipids play key role in keeping the cell integrity [27]. The main pathology in patients with recurrent oral ulcers and demonstrated changes in cholesterol profile would have an increased level of immunoglobulins and activated cytokines (low molecular weight polypeptide) such as tumor necrosis factor (TNF-α), interleukin-1 beta (IL-1β), soluble iL2 (sIL-2R), IL-6, chemokine IL-8 and T-immune medicated cells which play important role in immunity [27,28].

In this study, the level of cholesterol concentration with

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patients complaining of recurrent oral ulcers was taken together and it stated higher statistical significant.

Cholesterol Level in Relation to Recurrent Oral Ulcer

The present study revealed that there is statistically significant higher total cholesterol in the diseased group, this coincide with previous studies – which reported Total Cholesterol, Low Density Lipoprotein is found to statistically significantly higher in group with recurrent oral ulcer similar suggestion by Fedele et al., 2011 and Gulcan, 2015 [25,26].

It is also found High Density Lipoprotein Cholesterol were found significantly higher in patients with Recurrent Aphtous Ulcer in active stage [29].

Akoglu et al., 2013, found total serum cholesterol to be lower in patient with ulcer and Bilgili et al., 2012 note that there was no statistically significant total serum cholesterol between healthy and diseased [22].

Association of Blood Pressure in Relation to Recurrent Oral Ulcer

This study found that the control group had a stastically significant higher systolic blood pressure and coincide with Fedele et al., 2011 which observed oral mucosal disease patient were generally old age, with higher systolic and diastolic blood pressure [20], however we found to have no statistical significant difference in dialostic blood pressure.

Based on this research we have a clearer understanding of cholesterol in relation to the occurrence of oral ulcer, further studies can be conducted on the effect of controlling the cholesterol level in oral ulcer management and prevention.

Conclusion

In conclusion, this study had achieved its objectives. This study had found that there is relation between cholesterol level in patients with recurrent oral ulcer and association of blood pressure on recurrent ulcer patients.

Based on the results, there was a significant association between high level of cholesterol in patient with recurrent oral ulcer . It also shows that there is was a significant high systolic blood pressure and recurrent oral ulcer patient. However, it is believed that further work is required to investigate and explore more about the relationship between these variables.

As noted earlier future studies should include larger sample size. With a longer research time span it is possible to condut a longitudinal studies to further investigate on the cholesterol changes in the subject group.

It is also recommended to include more lab parameter as to give a further illumination on the specifics biomarker involves or implicated in oral ulcers disease, by studying HDL, LDL, TG and other lipids related components.

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