INTRODUCTION

The emerging pandemic of Non Communicable Diseases (NCDs) is creating a major health challenge globally. The burden of NCDs is also increasingly affecting developing countries such as Nepal. (STEPS 2013) Non communicable diseases (NCDs) cause 63% of deaths globally and nearly 80% of deaths in low and middle income countries. (WHO 2010) In Nepal, 42% of deaths are caused by NCDs and nearly 35% of deaths are caused by four particular NCDs: cardiovascular diseases (CVDs), cancer, chronic obstructive pulmonary diseases and diabetes mellitus. (Subedi 2007)

In 2002, the World Health Organization (WHO) identified eight major behavioral and biological risk factors for NCDs: tobacco use, harmful alcohol consumption, unhealthy diet, physical inactivity, overweight and obesity, raised blood pressure, raised blood glucose and abnormal blood lipids and its subset raised total cholesterol. (WHO 2002) These behavioral and biological risk factors contribute to chronic diseases and tobacco use has been found to be one of the leading preventable causes of premature death worldwide. (STEPS 2013, Brundtland 2000) In Nepal, the prevalence of smoking in men is around 27.0% and 10.3% in women, with men being started to smoke at 18.5 years and women at 17.6 years of age. Although bidi smoking is still practiced, manufactured cigarettes are the most common form of tobacco smoked, around 84.8% in Nepal. (STEPS 2013)

In developing countries like Nepal, young people are particularly vulnerable to initiation and addiction to consumption of different forms of tobacco and its products. The increasing trend of consuming tobacco might be due to the lack of knowledge, ignorance and weak policy towards tobacco cessation or increasing dependency towards consumption of tobacco.

Nicotine dependence is an addiction to tobacco products caused by one of its ingredients - the drug nicotine. It has been found that a cigarette on average contain 10mg of nicotine of which smokers typically absorbs 10% of it. (Benowitz, Jacob, Denaro and Jenkins 1991) The intake of tobacco both as smoked or smokeless form, give rise to physical and psychological dependency. (Hatsukami, Gust and Keenan 1987) In developed countries, approximately 30–40% of smokers
make an attempt to stop smoking in any year. However, without formal assistance, only about 2–3% of smokers making a quit attempt on their own, succeed in abstaining for at least a year. (Warnakulasuriya, Sutherland, & Scully, 2005) The state in the developing nation like Nepal is still more challenging.

More recently, it has been found that, although nicotine is the most important addictive component of tobacco smoke, it is probably not the only substance involved in the development of tobacco dependence.

Due to more rapid nicotine delivery in the body, cigarette smoking has higher dependence potential. One of the reasons that it is difficult to stop smoking may be because of the contribution of the non nicotine factors like the role of the object i.e., the cigarette itself; the habit and conditioning associated with smoking and the psychosocial aspects of smoking; explained as holding and caressing their cigarette pack can give some relief of stress. Offering a cigarette can be a means by which one contacts an unknown person. It can be a reason to take a break or pause from a boring task sometimes together with other smokers. This has the potential to increase bonding and togetherness. (Fagerström 2012) So it has been found difficult to refrain from the habit of consumption of smoking tobacco.

The increasing dependency towards tobacco and its products might result into its chronic use and be the cause for many non communicable diseases like potentially malignant oral diseases and cancer of oral cavity. To assess the tobacco dependency, Fagerström test for nicotine dependency (FTND) is the most widely accepted quantitative method. (Fagerström 1989) The score derived indicates the degree of nicotine dependence, the probable severity of withdrawal symptoms, degree of difficulty in achieving abstinence and possible speed of relapse. (Heatherton, Kozlowski, Frecker, Fagerström 1991; Kozlowski, Porter, Orleans, Pope and Heatherton 1994)

Nicotine dependence is a key barrier to smoking cessation and can be significantly alleviated by treatment (Fiore et al., 2000). Thus, it is vital to gather information about the correlates of nicotine dependence to allow planning of tobacco control programs.
In recent years, several biochemical markers have been used to explore tobacco use in epidemiological studies (Woodward, Tunstall, Smith and Tavendale 1991, Fendrich 2005). Cotinine is the most useful marker recognized for estimating the nicotine intake of cigarette smokers, because of its long half-life of 18–20 hours (Henningfield, Cohen and Pickworth 1993, Benowitz & Jacob 1994). The concentration of cotinine in blood, urine, or saliva is often used in research as an objective index of dependence because it provides an accurate measure of the quantity of nicotine consumed, which is itself a marker of dependence. (West 2004) One of the most frequently adopted biochemical measures of smoking is salivary cotinine levels, largely because of the non-invasiveness of the collection procedures, rapidity and their sensitivity and specificity. (Benowitz et al., 2002a) Salivary cotinine has a sensitivity of over 90% and >90% specificity in assessing smoking status. (Velicer, Prochaska, Rossi and Snow 1992; Murray, Connett, Lauger and Voelker 1993)

Tobacco and its metabolites are one of the major factors of various genetic damages in the body. The alteration in the epithelial cells of oral cavity is also a sign of genotoxic effect of the tobacco. As up to 90% of all cancers appear to be epithelial in origin, the buccal mucosa could be used to monitor early genotoxic events as a result of potential carcinogens entering the body through ingestion or inhalation. (Cairns 1975, Holland 2008, Rosin 1992) Exfoliated buccal epithelial cells have been used non-invasively to successfully show the genotoxic effects of lifestyle factors such as tobacco smoking, chewing of betel nuts and/or quids, medical treatments, such as radiotherapy as well as occupational exposure to potentially mutagenic and/or carcinogenic chemicals, and for studies of chemoprevention of cancer. (Holland 2008, Stich 1982, Stich 1983, Stich 1988) Occurrences of chromosomal damage in the oral epithelium can be evaluated using the micronucleus test. (Stich 1982) Micronuclei (MN) are induced in oral exfoliated cells by a variety of substances, including genotoxic agents and carcinogenic compounds in tobacco, betel nut, and alcohol. Tobacco-specific nitrosamines have been reported to be potent clastogenic and mutagenic agents which are thought to be responsible for the induction of chromatid/chromosomal aberrations resulting in production of MN. (Palve and Tupkari 2008). The induction of micronucleated cells by carcinogens and mutagens is a sign of the genotoxic effect of such substances. (Halder 2004) So the evaluation of the buccal
epithelial cell could be a potent marker to evaluate the genotoxic effect of tobacco and important biomarkers for the risk of cancer development. (Casartelli G 2000, Halder 2004, Saran 2008, Chatterjee 2009) Their frequency of occurrence is a measure of chromosome breakage in early cell divisions, and the number of micronuclei is known to increase with carcinogenic stimuli, long before the development of clinical symptoms. (Stich 1984)

This study is undertaken considering the increasing trend in consumption of tobacco and its products which could lead not only in increasing the rate of nicotine dependency but also the consecutive harmful effect in the body leading into various non communicable diseases. Reducing tobacco use and dependence has been identified as a key strategy in reducing the significant long-term health effects and associated economic costs of tobacco use. There are no such studies conducted in the Nepali population as per the indexed literature evaluating the dependency and its biochemical validation; and correlation with the genotoxic effect of tobacco.