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Original Article

# Iron expression in the biopsies of patients with different grades of OSCC

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## ABSTRACT:

Oral Squamous Cell Carcinoma (OSCC) is becoming a frequent problem all over the world and its etiological factors are different in different areas of the world. Iron is a pivotal nutrient and its deficiency is considered as malnutrition. The possibility that low iron intake might cause oral cancer needs to be investigated **Objective:** To evaluate the expression of iron in different grades of oral cancer. **Methods**: A total of 40 biopsy samples of OSCC were included in this study, comprising of 35% well and moderately differentiated and 25% in poorly differentiated cases. Iron staining was performed on all the cases and routine hematoxylin-eosin staining was also performed. Cases were then assessed by two independent hisptopathologists **Results:** Increased expression of iron in early stage of cancer was observed, which is well differentiated stage. Moderate expression was observed in moderately differentiated stage and almost no expression was observed in highly advanced stage of cancer which is poorly differentiated stage. **Conclusions:** According to this study, it has been concluded that there is more prevalence of oral cancer in males than in females because the males of this region are more involve in cigratte smoking and the use of oral drugs like pan, gutka, mishri and other types of chewing drugs. Iron deficiency in the body may lead to OSCC.

## KEYWORDS:
Oral squamous cells carcinoma, Iron expression, Malnutrition, Iron deficiency

## INTRODUCTION

Oral squamous cells carcinoma characterizes by the epithelial tumors in mouth and is the most common malignant tumor among all [1]. Oral and oropharyngeal squamous cell carcinoma comprehends 3% in men and 2% of total cancers in women. The rate of loss of life on large scale and number of deaths in a given period is 2% and 1% for men and women respectively. Oral Squamous Cell Carcinoma (OSCC) is more existing and occurring in old men. It may involve lip and internal structures and may show clearly with exophytic, endophytic, leukoplakic or erythroplakic act of appearing [2,3]. The clinical presentation in a classical way of head and neck squamous cell carcinoma is a shallow ulcer with heaped-up-edges, often covered by a plaque. The greater inducers (a molecule

that starts gene expression) of squamous cells carcinoma are all the forms of tobacco including smoked and smokeless. Since the last many decades, the survival rates of OSCC have not improved and creating a disappointing situation [4,5].

In Pakistan, the second most common cancer in males is oral cancer. In developed and developing countries, the incidence & prevalence of oral cancer is highest and increasing fastly [6]. In epidemiology & etiology of oral squamous cell carcinoma, the increasing rates of incidence & mortality has been observed. In men, the incidence rate is 6.6/100,000 while in women it is 2.9/100,000. The mortality rate of OSCC is 3.1/100,000 in men and 1.4/100,000 in women. The incidence and mortality rates related to OSCC is higher in men than in women [7,8]. In Karachi, increasing prevalence rates have been observed, along with some specific areas of Punjab and Sindh. In Punjab, highest rates have been noticed in Multan and in the case of Sindh it is observed in Jamshoro and much lesser frequency in North West Frontier Province [9]. Increase of considerable amount in rates of mortality have been noticed in most areas of eastern Europe especially in males of young age [10].

Iron is an exceedingly important nutrient of the human body that has the ability to proceed the formation of free radicals and helps in the process of redox cycling with many different roles in metastasis and in microenvironment. It requires for different complicated processes occurring vastly at molecular level and these processes cannot be revert such as $O_2$ around our body [11]. It facilitates cell proliferation and growth and due to its free radical formation & redox cycling capacity [12]. Which is directly associated with the growth and development of tumors. Iron metabolism reprogramming is considered as main prospect of tumor cell survival. The reason is that all pathways of iron storage, acquisition, efflux and regulation are agitated in cancer. iron metabolic pathways are also use for detecting prognosis and therapy of cancer. WNT pathways and signaling through hypoxia induced-factor (HIF) are main factors involved to alter iron metabolism [13].

Iron is also absorbed in the body from the dietary sources. The lining cells of intestines store iron as ferritin and ferroportin. Then ferritin transported in plasma in the form of transferrin [14]. Oxidative stress is the major reason behind the development of cancer cells [15,16]. iron accumulation also initiates oxidative stress. Alcohol and iron are involved in lipid peroxidation which directly linked with increased production of aldehydic products. Iron accumulation also trigger the activation of tumor necrosis factor-alpha and nuclear factor-kappa B which provide a favourable environment for carcinogenic compounds production. [17,18]. Generally iron overload is directly associated with cancer and this hypothesis is supported and accepted by many experiments, studies and human data. An overproduction of reactive oxygen species and free radicals could explain its oncogenic effect. Among the many factors (viral hepatitis, alcohol, tobacco etc.) which play a role in carcinogenesis, iron overload is probably an important one and therefore should be diagnosed and treated well especially at their early stages. Treated [19,20].

## METHODS

Overall, a study of oral biopsy samples was conducted, it consists of 40 cases of OSCC. Arrangement of sample collection had been made to get them from Mayo hospital, Lahore. Tissue submitted for histopathology must not be more than 3mm in thickness and not larger than the diameter of slides used. Most specimens from solid tissues were cut in the form of pieces measuring 10-15mm on the slides and 2-3mm in thickness. Hematology-Eosin staining as well as Iron staining was performed for all the cases. It was then assessed by two histopathologists.

## RESULTS

Pie chart shows the total number of cases according to grades. 35% cases were well differentiated, 40% cases were moderate differentiated while 25% were undifferentiated or poorly differentiated squamous cell carcinoma (Figure 1). Among well differentiated cases, 9/14 cases were iron positive, 2/16 in moderately differentiated and

0/10 in poorly differentiated (Figure 2). According to genderwise distribution, 8/30 males were positive while 3/10 females were iron positive (Figure 3). Overall, there were 27% cases iron positive (Figure 4).

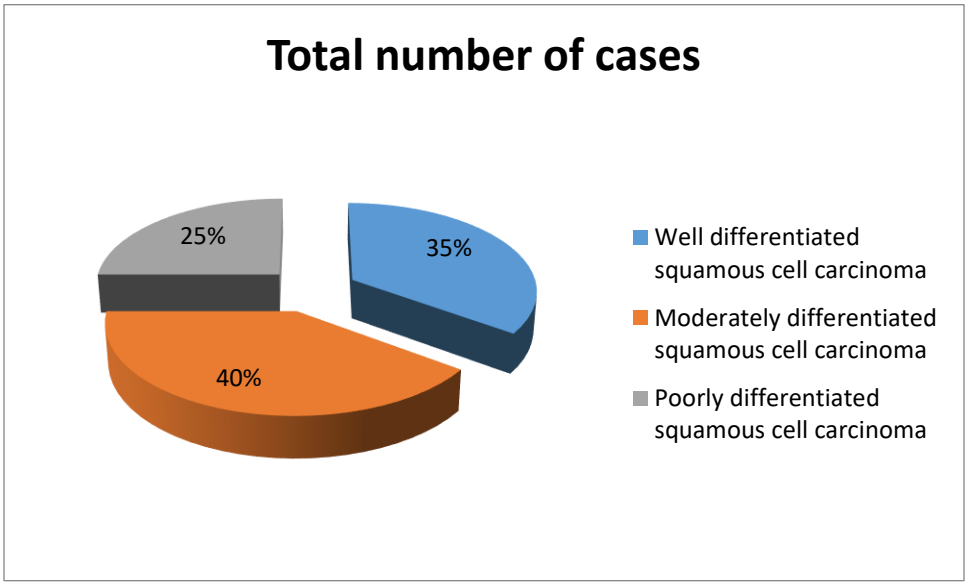


**Figure 1:** Total number of cases

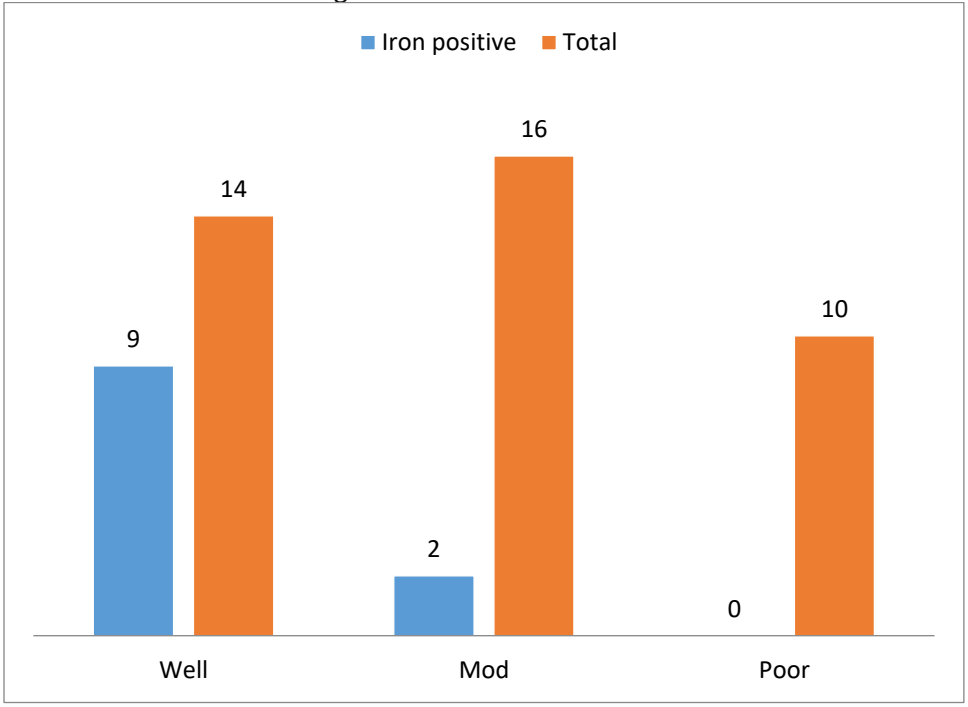


**Figure 2:** Iron positivity in different grades

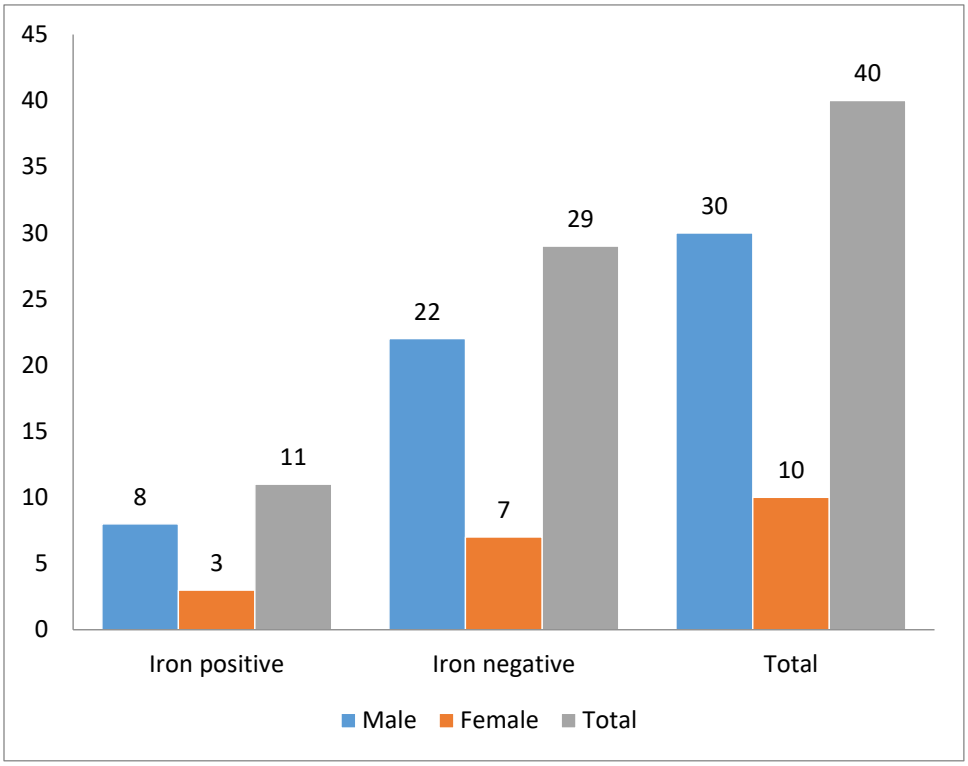


**Figure 3:** Genderwise distribution of OSCC cases according to iron expression

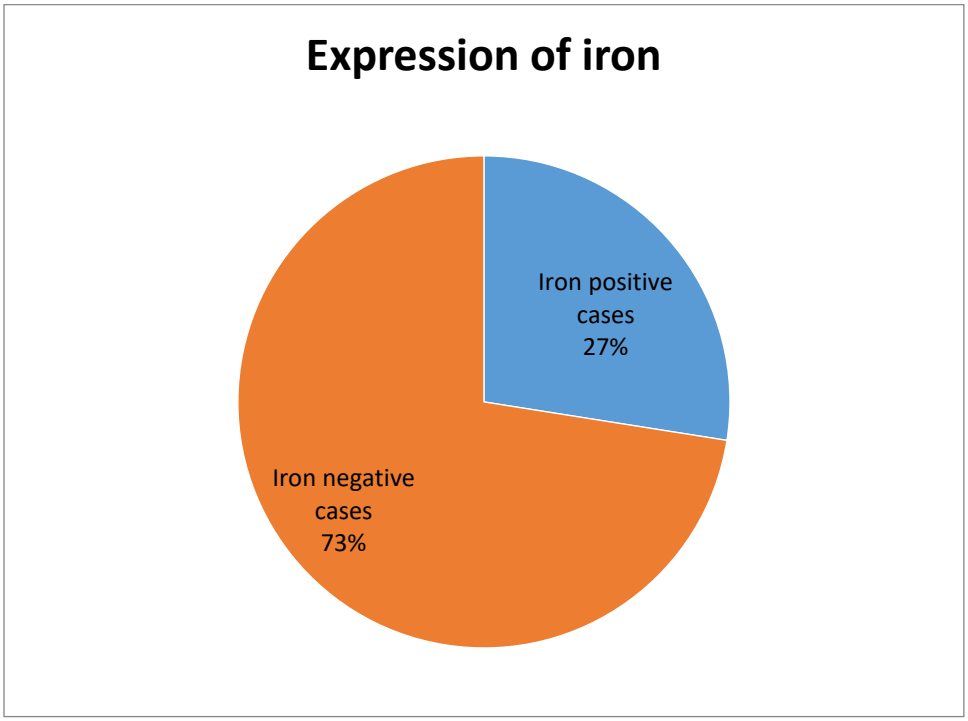


**Figure 4:** Distribution of OSCC cases according to iron expression

## DISCUSSION

Oral squamous cell carcinoma is becoming the problem in all over the world and its etiological factors are different in different areas of the world. Previously few studies have been reported regarding the expression of iron in different cancers and in oral squamous cell carcinoma. Iron deficiency also associated with oral cancer. The role of nutrition is not well understood, and one aspect of diet that has not been widely studied is iron metabolism. Iron is a pivotal nutrient and its deficiency is considered as malnutrition. The possibility that lows iron intake might cause oral cancer. Similar findings were seen in our study that increased expression of iron in early stage of cancer which is well differentiated stage. Moderate expression was observed in moderately differentiated stage and almost no expression was observed in highly advanced stage of cancer which is poorly differentiated stage.

## CONCLUSIONS

According to this study, it has been concluded that there is more prevalence of oral cancer in males than in females because the males of this region are more involve in cigarette smoking and the use of oral drugs like pan, gutka, mishri and other types of chewing drugs. We suggest to give iron supplements to the OSCC patients because the quantity of iron is decreased as the disease progresses. Because the amount of iron decreases as the proliferation of cancer cells increases. Iron is expressed strongly in the well differentiated squamous cell carcinoma. It proves that deficiency of iron in the body lead to the oral squamous cell carcinoma.

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