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THE ROLE OF CYP1B1 IN ORAL SQUAMOUS CELL CARCINOMA: A SYSTEMATIC REVIEW AND META-ANALYSIS

A. BARTAKE[1,2], G. SARODE[3], M. YUWANATI[4], B. NARANG[1], S. KAMBLE[1], S. SARODE[3]

[1]Department of Oral Pathology and Microbiology, Sinhgad Dental College and Hospital, Pune, Maharashtra, India
[2]Department of Oral Pathology and Microbiology, DY Patil Dental College and Hospital, Pune, Maharashtra, India
[3]Department of Oral Pathology and Microbiology, Dr. D.Y. Patil Dental College and Hospital, Dr. D.Y. Patil Vidyapeeth, Pune, Maharashtra, India
[4]Department of Oral Pathology and Microbiology, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai, Tamilnadu, India

Abstract – *Objective:* *CYP1B1 is crucial for the metabolism of tobacco-derived procarcinogens to reactive metabolites which is known to play a major role in the pathogenesis of oral squamous cell carcinoma (OSCC). The aim of the review was to know whether CYP1B1 gene is associated with OSCC risk.*

Materials and Methods: *The databases such as PubMed, Scopus, Web of Science, Cochrane Library, and Google Scholar were searched to synthesize evidence on the relationship between CYP1B1 and OSCC.*

Results: *Seven studies investigated CYP1B1 in 450 OSCC patients and 917 controls. Four studies have concluded that CYP1B1 is upregulated in OSCC, while three of the studies reported presence of polymorphism. Upregulation and downregulation of CYP1B1 was reported in three and two studies, respectively, while the remaining two studies reported differential presence of polymorphism. Different samples and methods were used for evaluation. Further, habits information was provided in a few studies. The most common polymorphisms were Arg48Gly, Ala119Ser, Leu432Val, and Ans453Ser. Overall, only four studies suggested CYP1B1 association with OSCC.*

Conclusions: *There is not sufficient evidence to suggest a clear association of CYP1B1 with OSCC. However, considering the clearly defined role of CYP1B1 in metabolizing pro-carcinogens like polycyclic aromatic hydrocarbons and phase I metabolism, there is need for well-designed cohort study.*

KEYWORDS: *Oral Squamous Cell Carcinoma, Oral cancer, CYP1B1, Cytochrome p450, Carcinogenesis.*

INTRODUCTION

The "cytochrome P450 (CYPs)" are a super family of enzymes which function as monooxygenases. In humans, CYP450 enzymes are found either in the mitochondria or in the endoplasmic reticulum of cells. They help in metabolizing endogenous and exogenous chemicals as well as potentially toxic compounds, like drugs and bilirubin. The cytochrome P450 gene subfamily CYP1 is important in the metabolism of drugs, steroids (especially oestrogen), and benzo[a]pyrene[1,2]. The CYP1B1 gene encodes an enzyme that activates a large number of polycyclic aromatic hydrocarbons (PAH's) and heterocyclic aromatic amines. In humans, CYP1B1 mRNA and protein are constitutively expressed in

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Corresponding Author: Monal Yuwanati, PhD; e-mail: monal9817@gmail.com

various organs such as the lungs, kidneys, and tissues regulated by estrogen such as the breast, ovary, and uterus. Due to its inherent ability to metabolize a number of human carcinogens, CYP1B1 has generated widespread interest in cancer research. In addition to this, CYP1B1 expression has also been shown in a wide range of tumors. Thus, it can be used as a tumour biomarker as well as a potential target for anticancer drugs[1,2].

Oral squamous cell carcinoma (OSCC) is one of the most common cancers occurring in the oral cavity. The etiology of OSCC is multifaceted and is dependent on various factors such as type, duration, dose, frequency, and method of application of the carcinogen. In addition, factors such as the host tissue susceptibility and the period of time for which the carcinogen is in contact with the tissue also play an important role in determining the cancer progression. Chronic exposure to carcinogens can induce genetic alterations and cause uncontrolled tumour growth.

Tobacco is a known causative agent in the development of OSCC. It exposes the oral epithelium to a variety of carcinogens such as nitrosamines and benzopyrenes, which known to induce oncogenic transformation. These carcinogens induce and upregulate the expression of both CYP1A1 and CYP1B1, which are part of the phase I detoxification enzyme system. It has been shown that transcriptionally activated CYP1B1 plays a very important part in the bioactivation of tobacco related procarcinogens to reactive metabolites as a product of phase I detoxification. Phase II detoxification system enzymes then detoxify these reactive metabolites. A strong association exists between impaired detoxification and carcinogenesis[1,2]. Overexpression/upregulation of CYP1B1 has been demonstrated in OSCC. However, Pradhan et al[3] reported contrasting observation. They observed downregulation of CYP1B1 in OSCC.

Although, CYP1B1 may be considered an important determinant of carcinogenesis, there is lack of clarity on its expression in OSCC. It is important to understand its association with OSCC to suggest it as target biomarker for drug therapy. Hence, we conducted systematic review to know whether the genotype status of polymorphisms in CYP1B1 gene is associated with oral squamous cell carcinoma risk.

MATERIALS AND METHODS

The present systematic review and meta-analysis was reported according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Systematic Review and meta-analysis (PRISMA 2020 checklist) (**Supplementary Table 1**).

Search Strategy and Source

The databases searched were PubMed, Scopus, Web of Science, Google Scholar (last search on 25 May 2022) (Figure 1). The literature search was conducted by using a combination of keywords such as "CYP1B1" or cytochrome P4501B1" and "oral cancer" or "oral carcinoma" or "oral cavity cancer" or "OSCC" or "oral squamous cell carcinoma" or "oral SCC" or "Head and Neck Cancer", which were used for the retrieval of the relevant papers. In addition, references were also checked from the bibliographies of relevant articles and included in this review. Studies evaluating the CYP1B1 expression in OSCC were included in this review. Conference proceedings and studies that are not associated with the OSCC were excluded from the analysis.

Study eligibility criteria

The population-intervention-comparator-outcomes-study design (PICOS) framework criteria was used to assess the eligibility of studies for inclusion: - Population: Human population irrespective of age, gender, and demographic restriction; - Condition/Comparator: Population with primary oral squamous cell carcinoma and healthy individuals; - Outcome: the outcome of interest was quantitative estimation of CYP1B1 gene expression in OSCC and health control tissue; - Study design: Systematic review included randomized, non-randomized studies, observational studies published in full text. Narrative, letters to the editor, case report, conference proceeding were excluded.

Data Extraction and Quality Assessment

Data was collected and the following variables were charted: year of publication, first author's country of origin, type of study, study population, methodology, and results. Two reviewers (AB & MY) independently charted the data, discussed the results, and updated the data-charting form. The included studies were assessed for quality using the Newcastle-Ottawa scale (NOS) quality assessment. Two authors (SS & GS) performed the quality assessment.

Statistical analysis

There was substantial heterogeneity and insufficient data for meta-analysis, hence, results synthesis was carried out without meta-analysis. Proportion analysis was carried out to find the pooled proportion effect size for upregulation of CYP1B1 in OSCC. Age, gender, habit, TNM stage, site association were analyzed using multivariate analysis in case of availability of sufficient data.

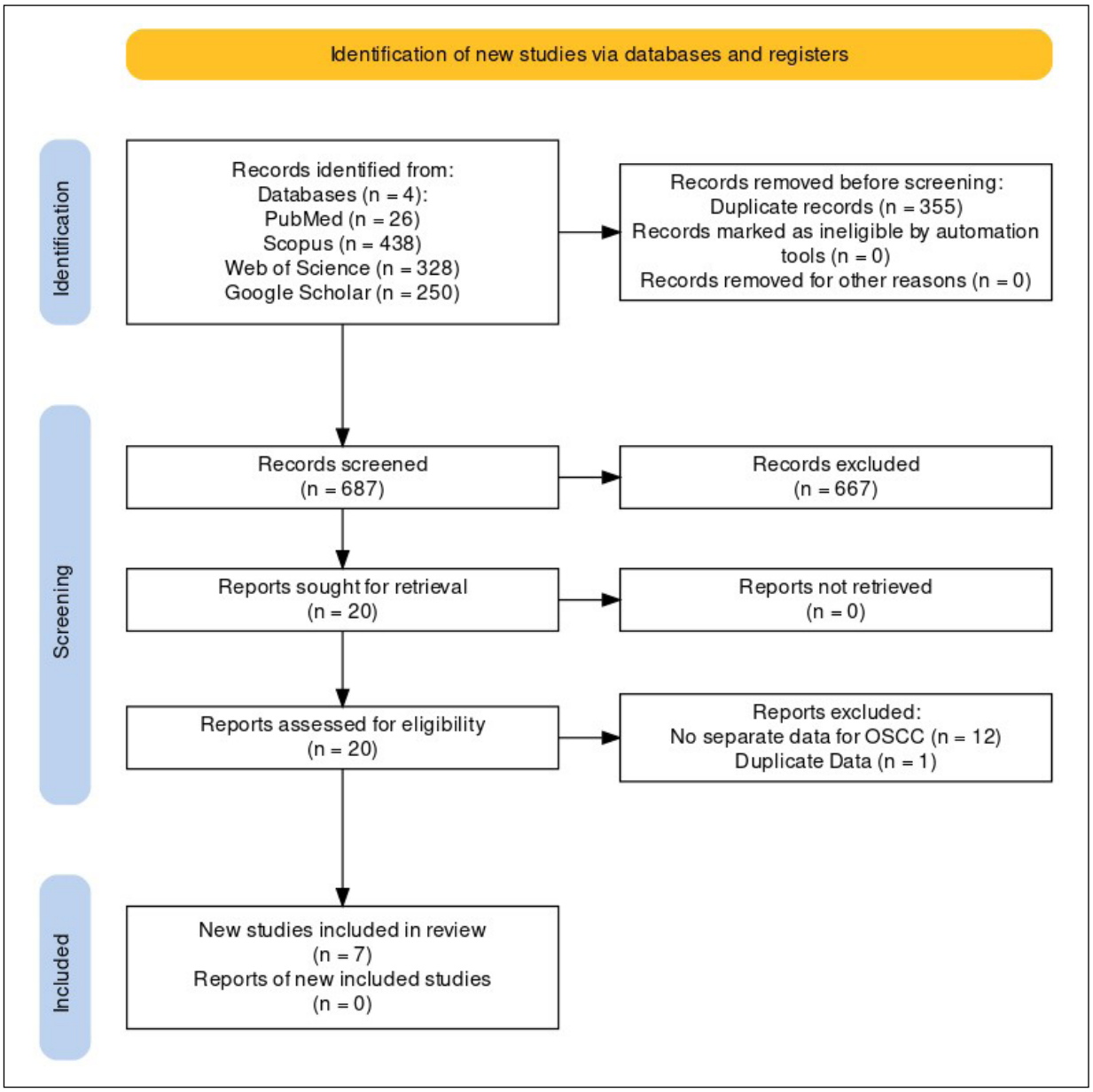

Fig. 1. Search, screening, and selection process of studies in systematic review and meta-analysis (PRISMA flow chart).

RESULTS

Search Results

A total of 1042 studies was found using online database searches, of which 687 were screened after eliminating the duplicates (Figure 1). A total of 667 was removed based on title and abstract. Twenty full-text studies were retrieved for further screening. Out of which, 13 studies were excluded based on eligibility criteria (**Supplementary Table 2**), leaving only seven studies for analysis (Figure 1).

Study characteristics

Detailed study characteristics were provided in Table 1. Only seven studies qualified for analysis[3-9]. Four studies were from India, two from USA, and one Brazil. The majority of studies did not provide complete details for OSCC and control population as well as required outcome measures. 450 OSCC patients and 917 controls were studied. OSCC samples were from 12 to 312. Out of seven studies, only Kaminagakura et al[8] study provided mean age (OSCC (34.7 yrs. [19-40]; Control (62.6 yrs. [50-90]) for OSCC and control.

TABLE 1. Characteristics of included studies.

Sr. No	Year	First Author	Country	Study Population	Sample Size	OSCC samples	Age (mean) of OSCC	Gender	Tobacco Habits	Sample Used for CYP1B1 analysis	OSSC (Upregulated/ Positive/ Total cases)	Control	Effect Size (OR/RR/ Prop)	Method	Upregulated/ Down-regulated/ Polymorphism	Supporting the Hypothesis
1	2017	Verma S	India	OSCC (Hospital)	OSCC-20; Control-20	20	NP	OSCC-20 (13M/7F); Control-20 (13M/7F)	–	Blood	17/20	–	–	PCR	Upregulated in OSCC (n=17)	Yes
2	2016	Kamina-gakura E	Brazil	OSCC	OSCC-41; Control-59	41	OSCC (34.7 [19-40]; Control (62.6 [50-90])	OSCC-27M/14F; Control-47M/12F	OSCC (TC31/ NTC8); Control (TC45/ NTC9)	Tissue (IHC)	NA	NA	RFS (Over-expression-64 %; Under-expression-25 %)	IHC	Differential	Yes expression
3	2014	Maurya SS	India	OSCC	OSCC-300 Control-750	300	NP	NP	OSCC (TC-160/ NC-140); Control (TC-240; NC-510) OSCC (S-208/ NS-92); Control (S-220; NS-530)	Blood	166/300 CYP1B1*2 [Control (W-350; Mt-399); OSCC (W-134; Mt-166)] CYP1B1*3 [Control-(W-446; Mt-303); OSCC-(W-200;Mt-100)] CYP1B1*2 [Control-(NTC-277; TC-135); OSCC-(NTC-81;TC-85)] CYP1B1*2 [Control-(NS-272; S-127); OSCC-(NS-127;S-115)] CYP1B1*3 [Control-(NTC-209; TC-94); OSCC-(NTC-50;TC-59)] CYP1B1*3 [Control-(NS-206; S-97); OSCC-(NS-35;S-77)]	– -	CYP1B1*2 [OR (1.0867; 95 % CI: 0.83 to 1.42)]a*; CYP1B1 *3 [0.7360; 95 % CI: 0.5557 to 0.9747]b**	PCR	Polymorphism Seen in OSCC (n=166)	No
4	2011	Shatalova EG	USA	Cell Lines/ OSCC	HNSCC-116; OSCC-25; Dysplasia-20; Control-37	25	NP	NP	NP	Tissue (IHC)	25/25 > Normal	37	NA	Tissue Micro-array; IHC; RT-PCR	Upregulated (25)	Yes
5	2011	Koloky-thas A	USA	OSCC Patients	OSCC-12	12	NP	NP	NP	Exfoliative cells	12/12 <Normal	3	NA	RT-PCR	Down-regulated (12)	No
6	2011	Pradhan S	India	OSCC	OSCC-51; Control-51	51	NP	NP	NP	Tissue (IHC)	Upregulation (5/51); downregulation (27/51); No difference (3/51); No expression (16/51)	35/51	NA	IHC	Down-regulated (28/36); Upregulation (5\36)	No
7	2009	Nagini S	India	OSCC	OSCC-20	20	NP	NP	OSCC (TC-20)	Tissue (IHC)	NA	NA	NA	IHC	Upregulated in OSCC (n=20)	Yes

Kaminagakura et al[8] and Verma et al[9] provided gender details (OSCC- 40 males and 21 females; control- 60 males/19 females). Tobacco habit details were also available for only few OSCC and control samples.

Study on genetic mutation or polymorphism requires the appropriate type of sample. Included studies were performed in blood (n=2) or tissue (n=4) or exfoliative cells (n=1). Out seven studies included, four studies used tissue (n=4), whereas one study used exfoliative cells[5]. Real Time-Polymerase chain reaction was the main gene analysis technique used for studying. Immunohistochemistry (IHC), tissue micro-array, western blot, as well as northern blot were other methods that evaluated CYP1B1 polymorphism in OSCC in these studies. We also found heterogeneity in samples, technique, and assessment criteria, which limited our analysis.

Association of CYP1B1 Polymorphism and OSCC

All studies aimed to correlate association of OSCC and CYP1B1. These studies indicated differential expression or presence of CYP1B1 polymorphism in OSCC. Three studies reported upregulation of CYP1B1 in their cohort whereas two reported down regulation (Table 1). Mourya et al[7] reported polymorphism in OSCC (n=166). At same time, Pradhan et al[3] reported downregulation. Overall, there is proof that CYP1B1 polymorphism is linked to OSCC. However, it was not possible to determine if the association was positive or negative due to insufficient data. The most commonly seen polymorphisms recorded are the Arg48Gly, Ala119Ser, Leu432Val and Ans453Ser polymorphisms.

Quality assessment

As per NOS, all studies were of good quality except two (Table 2). The population selection was appropriate in all studies. However, the samples size was less in most studies, which can have impact on CYP1B1 assessment in OSCC. Further, studies have not provided information on how sample size was determined. Despite the fact that normal persons served as controls in the studies, different samples were used for CYP1B1 assessment. Further, it is important that both OSCC and control patients must have similar or same exposure to ascertain its effect on outcome. Unfortunately, only three studies included the OSCC and control samples with similar i.e., tobacco exposure. Further, there was insufficient information for adjustment of confounders in study cohorts.

DISCUSSION

The present review mapped the available literature and identified a possible association between CYP1B1 and OSCC. CYP1B1 showed upregulation in OSCC which support its role as potential player in oral carcinogenesis. Majority OSCC patients have tobacco-associated habits, which coincide with upregulation of CYP1B1 enzyme in these patients. Port et al[10] reported similar observation where they observed increase levels of CYP1B1 mRNA in mucosa exposed to tobacco smoke. Normally, CYP1B1 help in detoxification of tobacco metabolites, hence, tobacco exposure should cause increase in levels. CYP1B1 causes activation of polycyclic aromatic hydrocarbons (PAH) into reactive metabolites which cause DNA damage. Longer tobacco exposure could stimulate higher expression of the CYP1B1 protein[8]. However, the studies observed downregulation of CYP1B1 that might be due to difference or absence of tobacco habits in those study OSCC cohorts. This raises the questions whether increase in levels of CYP1B1 mRNA should be associated with carcinogenesis or continuous maintenance of higher level of CYP1B1 in cells is required to induce the cancer. Assessment of CYP1B1 specifically in tobacco and non-tobacco cohort can ascertain this association. Mourya et al[7] evaluated the CYP1B1 gene in tobacco chewers and non-tobacco chewer. They observed increase in CYP1B1 in tobacco chewers. They reported high risk which was observed in cases who were regular smokers (4–8-fold) as compared to non-smokers. Similar findings were reported by Ruwali et al[11] that showed polymorphism in CYP1B1 is important in increase risk of HNSCC. In addition, synergistic effect of tobacco with other habits must be studied.

There is also differential expression of CYP1B1 in OSCC. Pradhan et al[3] observed predominantly downregulation of CYP1B1 in OSCC. However, studies found upregulation of CYP1B1 did not evaluate gene polymorphism. Gene polymorphism could be factor responsible for differential CYP1B1 expression. It has been observed that those individuals who were regular tobacco smokers and chewers carried the variant genotypes of CYP1B1 and are more prone to develop OSCC [12]. In the past few decades, several gene polymorphism in CYP1B1 has been linked to various cancers [13], which are mostly Single Nucleotide Polymorphisms (SNP)[14].

Among the most common SNPs of CYP1B1 gene, four have been known to be positively associated with OSCC. These include Arg48Gly (rs10012), Ala119Ser (rs1056827), Leu432Val (rs1056836) and Ans453Ser (rs1800440) polymorphisms.

TABLE 2. Newcastle - Ottawa Quality Assessment Scale (NOS) for the quality assessment (Adapted for Cross-sectional prevalence and control studies).

Author		*Verma S*	*Kaminagakura E*	*Maurya SS*	*Pradhan S*	*Kolokythas A*	*Shatalova EG*	*Nagini S*
Year	2017	2016	2014	2011	2011	2011	2009	
Selection	Oral squamous cell carcinoma patient Selection (1 Star)	*	*	*	*	*	*	*
	Sample size (1 Star)			*	*		*	
	Sampling Frame (1 Star)	*		*			*	
	Ascertainment of OSCC (1 Star)	*	*	*	*	*	*	*
Comparability	Selection of Control (2 star)	**	**	**	**	*	**	*
Exposure	Ascertainment of exposure (1 Star)	*	*	*	*	*	*	*
	Same method of ascertainment of exposure (1 Star)	*	*	*	*	*	*	*
	Adjusted for Confounder (2 Star)	*	*	*	*			
Total score (10)		8	8	9	8	5	8	5
Quality		Good	Good	Good	Good	Fair	Good	Fair

Thresholds for converting the Newcastle-Ottawa scales to AHRQ standards (good (7-10), fair (4-6), and poor 0-4): Good quality: 3 or 4 stars in selection domain AND 1 or 2 stars in comparability domain AND 3 or 4 stars in outcome/exposure domain: Fair quality: 1 or 2 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain Poor quality: 0 or 1 star in selection domain OR 0 stars in comparability domain OR 0 or 1 stars in outcome/exposure domain.

An increase in the frequency of the SNP's along with overexpression of CYP1B1 mRNA in the OSCC population could lead to increased formation of reactive intermediates, thereby increasing the risk of OSCC[15]. On the other hand, it has also been demonstrated that the association of SNP's in CYP1B1 and cigarette-smoking-induced OSCC was not statistically significant[16].

Though certain CYP1B1 haplotypes have recently been associated with OSCC, like the heterozygous genotype Ile/Valin codon 432 of CYP1B1, the role of polymorphisms of PAH-metabolizing CYP's in causing OSCC is still questionable. Another factor that may be considered is that the genetic alterations, which are seen during the development and later progression of OSCC, may not be equally distributed among the different sites of the head and neck region. In addition, polymorphisms seen in CYPs and their interactions with environmental risk factors such as tobacco or alcohol may influence the susceptibility to malignancy[17,18]. Given the scientific data available, it is safe to assume that the interactions of genes with the environment play an undeniable role in the development of cancers in the different sites of the head and neck. Similarly, the expression of CYP1B1 and its role in OSCC may also differ from site to site. Hence, CYP1B1 may be considered to be an important early biomarker for the risk of tobacco-induced OSCC development [7,19].

Furthermore, the risk multiplies with tobacco smoking, chewing, or alcohol consumption [20,21]. Because CYP1B1 expression is highly sensitive to the carcinogen benzo[a]pyrene (BaP) and tobacco-associated BaP-induced DNA binding is highly dependent on CYP1B1, CYP1B1 may be an early biomarker of OSCC[22,23]. CYP1B1 'Val432Leu' polymorphism may be a predisposing factor for smoking induced OSCC, and it is associated with an increased frequency of p53 mutations, which further adds credence to the fact that CYP1B1 polymorphism plays a major role in the development of OSCC[16]. BaP phenols are potent inducers of CYP1B1 and the enhanced expression of CYP1B1 has been shown to be indicative of oxidative DNA damage[4,24].

Contrary to the upregulation and polymorphism observed in various studies, a few studies have also reported CYP1B1 downregulation in OSCC at both the transcriptional and translational levels. The reason behind the observed down regulation of CYP1B1 in OSCC is not clear. One of the possible explanations can be that, as CYP1B1 is principally governed by the 'aryl hydrocarbon receptor (AhR)' and 'AhR nuclear translocator (ARNT) complex (AhR/ARNT)', any dysfunction or mutation in the same can lead to the down regulation of CYP1B1 in OSCC tissues[3]. Some studies have also claimed that there is no evidence of an association between the CYP1B1 Val432Leu polymorphisms and OSCC risk. CYP1B1Val-432Leu polymorphism may not have major effect, but could be a susceptibility factor in smokers [25].

Using appropriate technique for any gene regulation is important. Usually RT-PCR is the method of choice for detecting the gene expression. Majority studies used PCR/RT-PCR to identify gene expression as well as its variant. Few studies used the ELISA, IHC, Western blot technique, however, RT-PCR is considered as gold standard. Only one study used tissue microarray; although it's highly throughput it is expensive and require more time. Worldwide OSCC is an important health issue; hence, studying the carcinogenesis using the suitable and less expensive technique is warranted.

CONCLUSIONS

Though the role of CYP1B1 in metabolizing procarcinogens such as PAH's and its role in phase I metabolism is clearly defined, there is no sufficient evidence for CYP1B1 association with OSCC. Thus, there is still no clarity regarding the exact role of CYP1B1 in the pathogenesis of OSCC. Further studies exploring the genotypic and phenotypic expression of CYP1B1 in OSCC patients with a specific history of tobacco usage are required to establish if CYP1B1 has a definite role to play in the pathogenesis of OSCC.

Ethics approval:

As this is a systematic review and did not involve human subjects, ethics approval was not required.

Informed consent:

Not Applicable.

Conflict of Interest:

The authors declare that they have no conflict of interest to disclose.

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A.B., G.S., S.S. conceived the manuscript and revised it. M.Y., A.B, and B.N. did the statistical analysis, wrote the manuscript. S.K. prepared tables and figures, wrote manuscript.

ORCID ID:

Monal Yuwanati - 0000-0001-9233-8292; Sachin Sarode - 0000-0003-1856-0957; Gargi Sarode - 0000-0003-4628-8866.

Availability of data and materials:

The datasets generated and/or analyzed during the current study are available in the [PubMed, Web of Science, Scopus] repository.

REFERENCES

1. Murray GI, Melvin WT, Greenlee WF, Burke MD. Regulation, function, and tissue-specific expression of cytochrome P450 CYP1B1. Annu Rev Pharmacol Toxicol 2001; 41: 297-316.
2. Gonzalez FJ, Gelboin HV. Human cytochromes p450: Evolution and cDNA-directed expression. Environ Health Perspect 1992; 98: 81-85.
3. Pradhan S, Nagashri MN, Gopinath KS, Kumar A. Expression profiling of CYP1B1 in Oral Squamous cell Carcinoma: Counterintuitive downregulation in tumors. PLoS One 2011; 6: e27914.
4. Nagini S, Letchoumy PV, A T, CR R. Of humans and hamsters: A comparative evaluation of carcinogen activation, DNA damage, cell proliferation, apoptosis, invasion, and angiogenesis in oral cancer patients and hamster buccal pouch carcinomas. Oral Oncol 2009; 45: e31-e37.
5. Kolokythas A, Schwartz JL, Pytynia KB, Panda S, Yao M, Homann B, Sroussi HY, Epstein JB, Gordon SC, Adami GR. Analysis of RNA from brush cytology detects changes in B2M, CYP1B1 and KRT17 levels with OSCC in tobacco users. Oral Oncol 2011; 47: 532-536.
6. Shatalova EG, Klein-Szanto AJP, Devarajan K, Cukierman E, Clapper ML. 2011. Estrogen and cytochrome P450 1B1 contribute to both early- and late-stage head and neck carcinogenesis. Cancer Prev Res 2011; 4: 107-115.
7. Maurya SS, Katiyar T, Dhawan A, Singh S, Jain SK, Pant MC, Parmar D. 2015. Gene-environment interactions in determining differences in genetic susceptibility to cancer in subsites of the head and neck. Environ Mol Mutagen 2015; 56: 313-321.
8. Kaminagakura E, Caris A, Coutinho-Camillo C, Soares FA, Takahama-Júnior A, Kowalski LP. 2016. Protein expression of CYP1A1, CYP1B1, ALDH1A1, and ALDH2 in young patients with oral squamous cell carcinoma. Int J Oral Maxillofac Surg 2016; 45: 706-712.
9. Verma S, Saxena R, Siddiqui MH, Santha K, Sethupathy S. 2017. Evaluation of CYP1B1 expression, oxidative stress and phase 2 detoxification enzyme status in oral squamous cell carcinoma patients. J Clin Diagnostic Res 2017; 11: BC01-BC05.
10. Port JL, Yamaguchi K, Du B, De Lorenzo M, Chang M, Heerdt PM, Kopelovich L, Marcus CB, Altorki NK, Subbaramaiah K, Dannenberg AJ. 2004. Tobacco smoke induces CYP1B1 in the aerodigestive tract. Carcinogenesis 2004; 25: 2275-2281.
11. Ruwali M, Parmar D. 2010. Association of functionally important polymorphisms in cytochrome P450s with squamous cell carcinoma of head and neck. Indian J Exp Biol 2010; 48: 651-665.
12. Maurya SS, Anand G, Dhawan A, Khan AJ, Jain SK, Pant MC, Parmar D. 2014. Polymorphisms in drug-metabolizing enzymes and risk to head and neck cancer: Evidence for gene-gene and gene-environment interaction. Environ Mol Mutagen 2014; 55: 134-144.
13. Khlifi R, Messaoud O, Rebai A, Hamza-Chaffai A. Polymorphisms in the human cytochrome P450 and arylamine N-acetyltransferase: susceptibility to head and neck cancers. Biomed Res Int 2013; 2013: 58276.
14. Stoilov I, Akarsu AN, Alozie I, Child A, Barsoum-Homsy M, Turacli ME, Or M, Lewis RA, Ozdemir N, Brice G, Aktan SG, Chevrette L, Coca-Prados M, Sarfarazi M. 1998. Sequence analysis and homology modeling suggest that primary congenital glaucoma on 2p21 results from mutations disrupting either the hinge region or the conserved core structures of cytochrome P4501B1. Am J Hum Genet 1998; 62: 573-584.
15. Katiyar T, Maurya SS, Hasan F, Singh AP, Khan AJ, Hadi R, Singh S, Bhatt MLB, Parmar D. 2017. Association of cytochrome P450 1B1 haplotypes with head and neck cancer risk. Environ Mol Mutagen 2017; 58: 443-450.
16. Jorge-Nebert LF, Zhang G, Wilson KM, Jiang Z, Butler R, Gluckman JL, Pinney SM, Nebert DW. 2016. Head-and-neck squamous cell carcinoma risk in smokers: no association detected between phenotype and AHR, CYP1A1, CYP1A2, or CYP1B1 genotype. Hum Genomics 2016; 10: 1-17.
17. Soucek P, Susova S, Mohelnikova-Duchonova B, Gromadzinska J, Moraviec-Sztandera A, Vodicka P, Vodickova L. 2010. Polymorphisms in metabolizing enzymes and the risk of head and neck squamous cell carcinoma in the Slavic population of the central Europe. Neoplasma 2010; 57: 415-421.
18. Kolokythas A, Schwartz JL, Pytynia KB, Panda S, Yao M, Homann B, Sroussi HY, Epstein JB, Gordon SC, Adami GR. 2011. Analysis of RNA from brush cytology detects changes in B2M, CYP1B1 and KRT17 levels with OSCC in tobacco users. Oral Oncol 2011; 47: 532-536.
19. Chi AC, Appleton K, Henriod JB, Krayer JW, Marlow NM, Bandyopadhyay D, Sigmon RC, Kurtz DT. 2009. Differential induction of CYP1A1 and CYP1B1 by benzo[a]pyrene in oral squamous cell carcinoma cell lines and by tobacco smoking in oral mucosa. Oral Oncol 2009; 45: 980-985.
20. Harth V, Schafer M, Abel J, Maintz L, Neuhaus T, Besuden M, Primke R, Wilkesmann A, Thier R, Vetter H, Ko YD, Bruning T, Bolt HM, Ickstadt K. Head and neck squamous-cell cancer and its association with polymorphic enzymes of xenobiotic metabolism and repair. J Toxicol Environ Health A 2008; 71: 887-97.
21. Singh AP, Shah PP, Mathur N, Buters JTM, Pant MC, Parmar D. 2008. Genetic polymorphisms in Cytochrome P4501B1 and susceptibility to Head and Neck Cancer. Mutat Res - Fundam Mol Mech Mutagen 2008; 639: 11-19.
22. Nagaraj NS, Beckers S, Mensah JK, Waigel S, Vigneswaran N, Zacharias W. 2006. Cigarette smoke condensate induces cytochromes P450 and aldo-keto reductases in oral cancer cells. Toxicol Lett 2006; 165: 182-194.
23. Wen X, Walle T. 2005. Preferential induction of CYP1B1 by benzo[a]pyrene in human oral epithelial cells: Impact on DNA adduct formation and prevention by polyphenols. Carcinogenesis 2005; 26: 1774-1781.
24. Almahmeed T, Boyle JO, Cohen EG, Carew JF, Du B, Altorki NK, Kopelovich L, Fang JL, Lazarus P, Subbaramaiah K, Dannenberg AJ. 2004. Benzo[a]pyrene phenols are more potent inducers of CYP1A1, CYP1B1 and COX-2 than benzo[a]pyrene glucuronides in cell lines derived from the human aerodigestive tract. Carcinogenesis 2004; 25: 793-799.
25. Li G, Liu Z, Sturgis EM, Chamberlain RM, Spitz MR, Wei Q. 2005. CYP2E1 G1532C, NQO1 Pro187Ser, and CYP1B1 Val432Leu polymorphisms are not associated with risk of squamous cell carcinoma of the head and neck. Cancer Epidemiol Biomarkers Prev 2005; 14: 1034-1036.