KAI-1 ad p53 expression in Odontogenic cysts: An Immuno-histochemical Marker Study

Namrata Patil¹, Vijay Wadhwan², Minal Chaudhary³, Abhishek Singh Nayyar⁴

INTRODUCTION

The term cyst is derived from the Greek word “Kyistis” which means a bladder or sac. Kramer has defined cyst as ‘a pathological cavity having fluid, semi-fluid or gaseous contents and which is not created by the accumulation of pus’. Most cysts, but not all, are lined by epithelium. Like epithelium from elsewhere in the body, pathologic changes can and do occur within the cystic epithelium.[1] Odontogenic cysts are defined as those cysts which arise from the enamel organ or their remnants. Odontogenic cysts are lined by the epithelium derived from the remnants of the tooth forming organ, cell rests of Malassez, glands of Serres (cell rests of dental lamina), reduced enamel epithelium and sometimes, from the basal cell layers of the oral epithelia. During and after odontogenesis, these cell remnants remain as a common source of cystic changes within the jaw bones.[2,3] It is thought that the epithelial lining of the developmental odontogenic cysts has more proliferative potential than the epithelial lining of the inflammatory cysts. Radicular cyst is the most common cyst of inflammatory origin, is the most common cyst of inflammatory origin, arising associated with increased invasive ability of Oral Squamous Cell Carcinoma (OSCC) and as hypothesised for various odontogenic cysts and tumors. p53 protein functions in G1-S phase of the cell cycle to allow the repair of damaged DNA. In the present study, p53 and KAI-1 expression was investigated by using monoclonal antibodies in the various odontogenic cysts. Aims: To detect KAI-1 and p53 expression in Radicular cysts, Dentigerous cysts, and Odontogenic Keratocysts (OKCs) and to assess the relation between p53 and KAI-1 expression in the said cysts. Materials and Methods: The present study included histopathologically diagnosed cases of Radicular cysts, Dentigerous cysts, and Odontogenic Keratocysts (OKCs) for the expression of KAI-1 and p53 antibodies. Results: Amongst odontogenic cysts, radicular cysts expressed maximum positivity of KAI-1 (20.92%) while p53 positive cells were maximum in odontogenic keratocysts (4.04%). The correlation between KAI-1 and p53 expression in the various odontogenic cysts was not found to be significant. Conclusion: The increased KAI-1 expression in the radicular cysts and its downregulation in OKCs may be indicative of aggressive clinical behavior and the fact that OKCs are hypothesized as neoplastic rather than being developmental in origin.

Key words: KAI-1, p53, odontogenic cysts, OSCC, OKC, Monoclonal antibodies, Clinical behavior, Neoplastic origin.

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of several tumors (metastasis) as was observed by Guo et al who found upregulation of KAI-1 in early pancreatic carcinoma with its decreased expression in presence of metastasis.[7] Wu Q identified the role of KAI-1 in digestive tract carcinomas and predicted it to be a useful predictor of prognosis.[8] Farhadieh RD[9] and Imai Y[10] identified the role of KAI-1 in Oral Squamous Cell Carcinoma (OSCC) and suggested a decreased gene expression being associated with an increased invasive ability of OSCC. The expression of KAI-1/CD82 gene, inversely related to tumor progression, can thus be taken as a favorable prognostic indicator.[11]

At present, a number of oncogenes and tumor suppressor genes, including p53, RAS, β-catenin, and PTEN, have been implicated in various cancers.[12,13] p53 protein is a product of the tumor suppressor gene p53 which functions in the G1-S phase of the cell cycle to allow repair of the damaged DNA and to prevent the cell from entering the S phase, or alternatively, in guiding the damaged cells to apoptosis.[14-18] Also, the high recurrence rate and clinically aggressive behavior of odontogenic keratocysts have caused several investigators to study the cause for the same and expressions of KAI-1 and p53 protein in odontogenic keratocysts has remained one of the most sought topics in this regard assuming it to be associated with cell proliferation in the same.[19-21] Also the aforesaid features seen in these cysts have also caused several authors to regard it as a benign neoplasm rather than a cyst.[22-25] In the recent WHO classification (2005), on classification of odontogenic cysts and tumors, odontogenic keratocysts have been classified under benign tumors arising from epithelium and they have been renamed as keratinizing cystic odontogenic tumors.[22]

The expression of KAI-1 is supposed to decrease in cancer cell lines, also, OSCC. Cancer cells expressing KAI-1 attach to vascular endothelial cells through direct interaction between KAI-1 and DAR (an endothelial cell surface protein) leading to inhibition of tumor cell proliferation and induction of senescence.[25,26] The tumor metastasis is suppressed mainly by an inhibition of cancer cell motility and invasiveness.[26-27]

As odontogenic keratocysts have recently been categorized as benign neoplasms with high recurrence rates as high as 60%,[20,21-25], an attempt was made to explain the differences on the basis of its expression of KAI-1 and p53. In the present study, immunohistochemistry for KAI-1 and p53 was employed to evaluate the cell proliferation and aggressive behavior in the radicular, dentigerous and odontogenic keratocysts. There are no such studies as such, conducted in relation to odontogenic cysts, and this was first of its kind of studies. Before this, the expression of KAI-1 ad p53 has been studied in relation to the various malignancies. So, this study was designed to study the expression of KAI-1 ad p53 in odontogenic cysts and in particular, to get an explanation for the neoplastic behavior of Odontogenic Keratocysts, for, whether any correlation existed. In the present study, p53 and KAI-1 expression was investigated by using monoclonal antibodies in the various odontogenic cysts. This study actually tries to compare the expression of the abovementioned genes in odontogenic cysts comparing the clinical implications as against OSCC, a condition wherein the expression of the said genes has already been discussed in detail with various hypotheses proposed as the possible role they might have in OSCC.

The aims of the study were to detect KAI-1 and p53 expression in Radicular, Dentigerous, and Odontogenic Keratocysts (OKC) and to get an explanation for the neoplastic behavior (biologically aggressive behavior) of Odontogenic Keratocysts, for, whether any correlation existed.

MATERIALS AND METHODS

An immunohistochemical study was carried-out for the evaluation of KAI-1 and p53 expression in the various odontogenic cysts which comprised of radicular cysts, dentigerous cysts and odontogenic Keratocysts.

Paraffin embedded sections were obtained. The study sample consisted of 30 cases of radicular cysts, 27 cases of dentigerous cysts, 37 cases of OKCs, and 10 cases of normal buccal mucosa. The immunohistochemically stained tissue sections were evaluated by counting approximately 1000 cells in high power field wherever possible. The tissues which yielded insufficient epithelial lining as in some of the cases of dentigerous cysts, the total numbers of cells were counted and the labeling index was obtained. Staining was observed as nuclear and cytoplasmic membrane staining. Tissue sections positive for KAI-1 and p53 were examined for the presence of brown stained cytoplasm and evaluated by locating the epithelial linings most heavily labeled by scanning the sections at a 100X magnification. Cell counts were made at 400 X magnification with conventional light microscope in 5 randomly selected fields. KAI-1 and p53 labeled cell counting was done amongst all groups. The constituent cells of the lining epithelium were divided into basal, suprabasal/intermediate and surface layers. Cuboidal/columnar cells located in one row at the basement membrane were considered as the basal layer. The surface layer constituted the flattened or polygonal cells consisting of one to five layers, localized just underneath the surface of the lining epithelium. The suprabasal/intermediate layer was composed of relatively large round cells between the basal and the surface layers. The numbers of positively stained nuclei were expressed as a percentage of the total number counted for individual layer and in complete epithelium.

Number of IHC Positive Cells (KAI-1/p53) x 100

KAI-1/p53 labeling index = Total number of cells observed

KAI-1 expression in the epithelium was converted into score defined by Farhadieh RD et al[10] with score 1 assigned for <10% of cells with positive staining, 2 for 11-30%, 3 for 31-50% and 4 for >51% of the total number of cells with positive staining. The cells which were positive for KAI-1 expression were divided according to their scores.

The study was approved by the Institutional Ethics Committee before commencement of the study. The results were presented in two sections with detailed analysis of KAI-1 expression as descriptive statistics and significant differences in the group. Similar results were applied for p53 expression and the statistical analysis was carried-out.

Principle of immunohistochemical staining: Sections were hydrated with increasing grades of alcohol and brought to distilled water and treated with hydrogen peroxide (H₂O₂) to eliminate endogenous peroxidase activity. The tissues were then incubated sequentially with:

- Primary antibody (KAI-1, C-16, sc-1087, primary antibody, rabbit polyclonal anti-human antibody, Santa Cruz Biotechnology, Inc., p-53, clone DO-7, primary antibody, mouse monoclonal anti-human antibody, DAKO), which binds to specific tissue antigens;
- Secondary antibody (Biotinylated secondary antibody, DAB Chromogen, DAB Substrate Buffer, Hematoxylin, DAKO), which binds to the primary antibody; it is a polyvalent antibody that will bind to primary antibodies derived from rabbit, mouse, rat and guinea pig; and
- Addition of peroxidase substrate (hydrogen peroxidase) and chromogen results in the formation of a colored precipitate at the tissue antigen sites. Counter staining with hematoxylin aided in visualization.

Positive and negative controls

Normal oral mucosa samples showing KAI-1 labeling for p-53 expression acted as a positive control. One positive control was included for each immunohistochemical cohort. One section from each positive control was used as the negative control by omitting the primary antibody and by incubating with Tris-Buffered Saline (TBS).

Statistical Analysis
Table 1: One-Way Anova for KAI-1 and p53 expression in the epithelial lining of Radicular cysts, Dentigerous cysts, OKCs and Normal Buccal Mucosa

<table>
<thead>
<tr>
<th>Variable</th>
<th>Sum of Squares</th>
<th>df</th>
<th>Mean Square</th>
<th>F</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>KAI-1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Between Groups</td>
<td>16419.58</td>
<td>4.00</td>
<td>4104.89</td>
<td>31.91</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td>Within Groups</td>
<td>16596.84</td>
<td>129.00</td>
<td>128.66</td>
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</table>

<table>
<thead>
<tr>
<th>Variable</th>
<th>Sum of Squares</th>
<th>df</th>
<th>Mean Square</th>
<th>F</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>p53</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Between Groups</td>
<td>81065.60</td>
<td>4.00</td>
<td>20266.40</td>
<td>413.00</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td>Within Groups</td>
<td>6330.18</td>
<td>129.00</td>
<td>49.07</td>
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</tr>
</tbody>
</table>

** Highly significant at p<0.001

Table 2: LSD (Least Significant Difference) Post-Hoc test analysis between KAI-1 expression in Radicular cysts, Dentigerous cysts, OKCs and Normal Buccal Mucosa

<table>
<thead>
<tr>
<th>Variable 1</th>
<th>Variable 2</th>
<th>Mean</th>
<th>Std. Error</th>
<th>p-value</th>
<th>95% Confidence Interval (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Radicular Cyst</td>
<td>Dentigerous Cyst</td>
<td>2.54</td>
<td>3.01</td>
<td>0.40</td>
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<tr>
<td></td>
<td>Radicular Cyst</td>
<td>Normal Mucosa</td>
<td>9.91</td>
<td>2.79</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td></td>
<td>Dentigerous Cyst</td>
<td>OKC</td>
<td>-3.36</td>
<td>4.14</td>
<td>0.42</td>
</tr>
<tr>
<td></td>
<td>Dentigerous Cyst</td>
<td>Normal Mucosa</td>
<td>7.37</td>
<td>2.87</td>
<td>0.01*</td>
</tr>
<tr>
<td></td>
<td>OKC</td>
<td>Normal Mucosa</td>
<td>-5.90</td>
<td>4.20</td>
<td>0.16</td>
</tr>
</tbody>
</table>

*significance at p<0.05 ** Highly significant at p<0.001

Statistical analysis was performed with SPSS (version 13, SPSS Inc., Chicago, USA) package. The statistical tests used for the analysis of the results were:

Descriptive statistical analysis;
One-way Anova;
LSD (Least Square Difference method);
Chi-square test for inter-group comparisons; and
Independent t-test.

RESULTS

KAI-1 counts were observed in decreasing order in the normal buccal mucosa with a mean of 24.28 (± 4.15), followed by Radicular cysts with a mean of 20.92 (± 4.68), Dentigerous cysts with mean of 18.38 (± 4.17) and OKCs with mean of 11.01 (± 13.01). Descriptive statistics was, also, performed for the expression of p53 in the aforementioned cysts and control groups. Statistically significant variations of means of p53 labeling indices were found amongst all groups. p53 counts were observed in increasing order in OKCs with a mean of 4.04 (± 4.13), normal buccal mucosa 3.44 (± 2.32), Radicular cysts 0.45 (± 0.72) and Dentigerous cysts 0.16 (± 0.37). One way analysis of variance (ANOVA) showed highly significant variation (p=0.00) of the mean squares 4104.89 between groups and 128.66 within groups with the degree of freedom between groups (df=4.00) and within groups (df=129.00) in case of KAI-1 expression in epithelium of Radicular cysts, Dentigerous cysts, OKCs and Normal mucosa. F-value of 31.91 was obtained showing that statistically significant variations of means of the labeling indices were found amongst all the groups. (Table 1) One way analysis of variance ANOVA in case of p53 expression in epithelium of Radicular cysts, Dentigerous cysts, OKCs and Normal buccal mucosa, also, revealed highly significant variation (p=0.00) of the mean squares 20266.40 between groups and 49.07 within groups with the degree of freedom between groups (df=4.00) and within groups (df=129.00). (Table 1) The LSD post-hoc test for KAI-1 expression in Radicular cysts, Dentigerous cysts, OKCs and Normal buccal mucosa, also, came-out to be highly significant in all the compared groups except between the expression in Radicular and Dentigerous cysts, Radicular cysts and Normal buccal mucosa and Dentigerous cysts and Normal buccal mucosa (p=0.05) (Table 2) The LSD post-hoc test in case of p53 expression was though not found to be significant in the compared groups with p>0.05 (Table 3) 100% positivity was noted for KAI-1 expression in Radicular and Dentigerous cysts while OKCs showed a positivity in 22 (59.45%) of the cases and 15 cases were found to be negative for KAI-1 staining. There were significant differences observed in the Radicular and Dentigerous cysts and OKCs. Regarding p53 expression, 10 cases of Radicular cysts out of 30, 6 of Dentigerous cysts and 31 of OKCs were positive (83.78%). OKCs showed the highest positivity of 83.78 % as compared to Radicular and Dentigerous cysts which showed a positivity of 33.33% and 22.22% respectively. Also, KAI-1 and p53 expressions were compared between each group and came-out to be statistically significant (p=0.00). (Table 4)

DISCUSSION

Odontogenic cysts are comprised of an unusually diverse group of lesions because odontogenesis is a complicated process in which cells in various stages of differentiation participate in a complex, pre-determined manner, constituting a group of frequent intra-osseous lesions in the jaw bones.[1-3] Unlike the radicular and dentigerous cysts, the odontogenic keratocysts can assume a clinically aggressive and destructive behavior.[4,5] If inadequately treated, these cysts cause considerable expansion within and damage the jaw bones. A significant clinical problem is the high recurrence rate (12.65%) observed following surgical enucleation in these cysts.[6,19]

When a cyst grows, multiple cytokines are liberated, such as Interleukins (ILs), Tumor Necrosis Factor (TNF), Matrix Metalloproteinases (MMPs), tenasin, fibronectin and Parathyroid-Hormone-related Proteins (PTH-rPs) which modulate the function of other cell types and are involved in cellular immune and inflammatory responses via auto- and para-crine signaling leading to extensive bone damage.[24] Odontogenic keratocysts (OKCs) are characterized by their epithelial lining that has some intrinsic growth potential, added to which, inflammation alters not only the morphology but also the proliferative potential of the epithelial lining.[25,26] The keratinocytes synthesize IL-1 and IL-6 and these cytokines and TNF account for raised levels of PGs and collagenase synthesis by uninflamed cystic linings. Also, Parathyroid-Hormone-related Proteins (PTH-rPs) have been hypothesized to be expressed in high levels in OKCs and to play a possible role in the growth of these cysts and bone resorption seen by acting synergistically with IL-1.[24] Different markers like proliferating cell nuclear antigens (PCNAs), p53, Ki-67, Silver nucleolar organizer regions (AgNoR) have been studied in odontogenic cysts with PCNAs denoting aggressiveness in such lesions.
Table 3: LSD (Least Significant Difference) Post-Hoc test analysis between p53 expression in Radicular cysts, Dentigerous cysts, OKCs and Normal Buccal Mucosa

<table>
<thead>
<tr>
<th>Variable1</th>
<th>Variable2</th>
<th>Mean</th>
<th>Std. Error</th>
<th>p-value</th>
<th>95% Confidence Interval (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Upper bound</td>
</tr>
<tr>
<td>Radicular Cyst</td>
<td>Dentigerous Cyst</td>
<td>0.28</td>
<td>1.86</td>
<td>0.88</td>
<td>-3.39</td>
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<tr>
<td>Radicular Cyst</td>
<td>Normal Mucosa</td>
<td>-2.99</td>
<td>2.56</td>
<td>0.24</td>
<td>-8.05</td>
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<td>Dentigerous Cyst</td>
<td>OKC</td>
<td>-3.88</td>
<td>1.77</td>
<td>0.03</td>
<td>-7.39</td>
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<tr>
<td>Dentigerous Cyst</td>
<td>Normal Mucosa</td>
<td>-3.27</td>
<td>2.59</td>
<td>0.21</td>
<td>-8.40</td>
</tr>
<tr>
<td>OKC</td>
<td>Normal Mucosa</td>
<td>0.61</td>
<td>2.50</td>
<td>0.81</td>
<td>-4.33</td>
</tr>
</tbody>
</table>

Table 4: Comparison between KAI-1 and p53 expression in different groups by independent t-test

<table>
<thead>
<tr>
<th>Sample</th>
<th>Variables</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>Std. Error Mean</th>
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<th>p-value</th>
<th>95% Confidence Interval (CI)</th>
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<tbody>
<tr>
<td></td>
<td>KAI-1</td>
<td>20.92</td>
<td>4.68</td>
<td>0.86</td>
<td>23.66</td>
<td>&lt;0.001**</td>
<td>18.71</td>
</tr>
<tr>
<td></td>
<td>p53</td>
<td>0.45</td>
<td>0.72</td>
<td>0.13</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Dentigerous cyst</td>
<td>KAI-1</td>
<td>18.38</td>
<td>4.17</td>
<td>0.80</td>
<td>22.59</td>
<td>&lt;0.001**</td>
<td>16.56</td>
</tr>
<tr>
<td></td>
<td>p53</td>
<td>0.16</td>
<td>0.37</td>
<td>0.07</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>OKC</td>
<td>KAI-1</td>
<td>11.01</td>
<td>13.01</td>
<td>2.14</td>
<td>3.10</td>
<td>&lt;0.001**</td>
<td>2.44</td>
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<tr>
<td></td>
<td>p53</td>
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<td>4.13</td>
<td>0.68</td>
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<tr>
<td>Normal Mucosa</td>
<td>KAI-1</td>
<td>24.28</td>
<td>4.15</td>
<td>1.31</td>
<td>13.86</td>
<td>&lt;0.001**</td>
<td>17.62</td>
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<td></td>
<td>p53</td>
<td>3.44</td>
<td>2.32</td>
<td>0.74</td>
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** Highly significant at p<0.001

entire epithelial lining exhibiting KAI-1 reactivity and it was intense in areas of inflammation [Figure 1] indicating KAI-1 expression to be upregulated in lesions with inflammation. In dentigerous cysts, KAI-1 positivity was seen throughout the thickness of the epithelium. Staining was seen as distinct membranous or, cytoplasmic involving the epithelium lining [Figure 2] clearly evident even in areas of minimal inflammation and places of diffuse inflammation indicating KAI-1 upregulation being not just a phenomenon associated with inflammation but other factors, too, including the variable cytokines liberated by the cystic linings. In odontogenic keratocysts, only 83.78% of the cases showed positivity for KAI-1. Positivity was noticed in the superficial layers and tended to be focally or, diffusely positive and was least in the basal cell layers and suprabasal layers which exhibited absence of KAI-1 expression [Figure 3]. Some of the keratocystic linings in which inflammation was minimal exhibited negligible or, absence of staining. Not much has been reported about the KAI-1 expression in odontogenic cysts and there has been a paucity of studies in the literature regarding the expression of KAI-1 in the odontogenic apparatus. Extensive search revealed one study conducted by G Iezzi et al[29] where the authors found a positive KAI-1 expression in radicular and dentigerous cysts but very little expression in odontogenic keratocysts amongst which none of the parakeratinized OKCs showed positivity and only 4 out of 16 orthokeratinized OKCs revealed KAI-1 positivity. Our results are in partial agreement with their study as KAI-1 expression in dentigerous and radicular cysts were nearly comparable with their studies although OKCs exhibited KAI-1 positivity to a lesser extent.

There is a documented proof that downregulation of KAI-1 gene is associated with increased metastasis. So, taking the reverse also to be true, any lesion which is benign in nature, is supposed to express KAI-1, depending on the level of its aggressiveness. The term Odontogenic Keratocyst (OKC) designates a cyst with a characteristic histological appearance and a specific clinical behavior. The epithelium of OKCs is believed to have an intrinsic growth potential and shows strong evidence of being neoplastic rather than developmental origin.[22,23] OKCs also share allelic loss of the same loci that have been implicated in the development of OSCCs providing further proof regarding its being neoplastic in nature. [22,23] Thus, results of our study show that although in radicular [Figure 1] and dentigerous cysts [Figure 2], there was positivity to KAI-1, in OKCs [Figure 3], there was significantly less expression. This lack of KAI-1 expression in OKCs could help to explain the differences in the clinical and pathological behavior of OKCs, and according to what seems to be the pattern in several types of epithelial tumors, could be related to the increased aggressive behavior, invasiveness and high frequency of the recurrences found in OKCs. An increase in cell proliferation plays an important role in the development of odontogenic cysts.
p53 protein is a product of the tumor suppressor p53 gene which functions in G1-S phase of the cell cycle to allow repair of the damaged DNA. p53 gene has a shorter life in normal cells and cannot be detected immunohistochemically but when mutated, the p53 protein becomes more stable and detectable. Therefore, p53 protein is expressed in actively proliferating cells. While positive staining for p53 may be correlated with genetic mutation, the wild protein can also be retained in the tissues by, for example, binding to other proteins or, due to some defects in the normal degradation pathway and can therefore be identified by immunohistochemistry. Wild type p53 protein acting as a tumor suppressor downregulates cell growth, but mutation in p53 can inactivate its tumor suppression activity allowing the dominant oncogenic factors to lead to malignant transformation.\cite{16-18}

In the present study, OKCs showed 83.78% p53 positivity as against radicular and dentigerous cysts which showed 100% positivity for p53. p53 immunolabelling was dense and scattered in the basal and suprabasal cell layers in OKCs [Figure 4], whereas very few densely stained cells were located in the basal cell layers in radicular [Figure 5] and dentigerous cysts [Figure 6] and normal oral mucosa. p53 expression was highest in OKCs [Figure 4]. In radicular [Figure 5] and dentigerous cysts [Figure 6], most of the p53 positive cells were located in the basal and suprabasal cell layers. This was in agreement with the study conducted by Ogden et al who concluded that most of the p53 positive cells were located in the basal cell layers in OKCs whereas radicular and dentigerous cysts were negative for p53.\cite{90} Slootweg et al\cite{31} and Li TJ et al\cite{32} however, reported that positive cells were detected in all odontogenic cysts, though to variable extents. The findings of the present study were in accordance with these authors as well as with the various other studies present in the literature.\cite{20,27,28,33,34}

Recent studies have also indicated that p53 alteration occurs at a greater frequency in invasive than in non-invasive carcinomas.\cite{15,35} The high reactivity of p53 protein in OKCs could thus be related to the factors peculiar to the extensive cystic lesions including their locally aggressive behavior, high mitotic activity of their cells and their tendency to recur, although the rate of recurrence, might depend on the method and adequacy of their treatment. This p53 reactivity thus indicates the possible role, it carries, in the high intrinsic growth potential and biological aggressiveness of these lesions.
REFERENCES


CONCLUSION

Although a large body of work exists regarding the significance of p53 expression, the significance of increased or decreased KAI-1 expression in the aggressiveness in non-neoplastic lesions remains as yet unclear. This study thus paves way for further studies to be conducted to investigate, if any, correlation existed between KAI-1 and p53 expressions in these odontogenic cysts and numerous other odontogenic lesions with respect clinical behavior as very limited studies, till date, have been conducted in this regard.

ACKNOWLEDGEMENT

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CONFLICTS OF INTEREST

No conflict of interest are declared.
Patil et al.: Expression of KAI-1 and p53 in Odontogenic Cysts: An IHC Study


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