Original Article

Immunohistochemical evaluation of Glut1 in dentigerous cysts, odontogenic keratocysts, and ameloblastoma

Deepika K, N. Govind Raj Kumar, A. Sudarshan Kumar, Roja Lakshmi Karri

Department of Oral and Maxillofacial Pathology, GSL Dental College, Rajahmundry, Andhra Pradesh, India

Abstract

Context: Glucose uptake may be considered the rate-limiting step for the growth and metabolism of the cancer cell. Studies on GLUT1 have shown that GLUT1 is involved in cell survival and proliferation in both healthy and pathological circumstances. GLUT1 expression is regarded as one of the crucial elements in the development of local aggressiveness, tumour invasiveness, and metastasis, particularly in malignant tumours. The role of glut1 in odontogenic cysts and tumours has remained uncertain.

Aim: The aim of the study is to assess the expression of Glut1 in dentigerous cysts, odontogenic keratocysts, and ameloblastoma.

Settings and Design: The study was conducted in GSL Dental College. The study design was a resprospective immunohistochemical study.

Methods and Material: Formalin-fixed, paraffin-embedded blocks of histologically confirmed cases (n = 50), 10 cases of odontogenic keratocysts, dentigerous cysts, ameloblastomas solid, ameloblastomas unicystic, and dental follicles each. Brown colour staining was considered as positive staining for GLUT1. Quantitative analysis was performed by counting the number of labelled cells, and semi-quantitative analysis was conducted by assigning immunostaining intensity scores.

Statistical Analysis: Chi-square test was used to compare differences between the groups. A *P* value of ≤ 0.05 was considered as statistically significant.

Results: Odontogenic keratocysts and unicystic ameloblastoma showed $\geq 50\%$ of label cells with strong intensity of staining. Odontogenic keratocysts and solid ameloblastoma showed sub-cellular localisation of staining in the cytoplasm and membrane. Dentigerous cysts exhibited combined nucleus, cytoplasm, and membrane sub-cellular localisation of staining.

Conclusions: The development of ameloblastomas, odontogenic keratocysts, and dentigerous cysts appears to be influenced by GLUT-1. Variation in its expression may aid in explanation of some of the differences in biological activity of these lesions.

Keywords: Ameloblastoma, dentigerous cyst, Glut1, odontogenic keratocysts

Address for correspondence: Dr. Roja Lakshmi Karri, Department of Oral and Maxillofacial Pathology, GSL Dental College, Rajahmundry, Andhra Pradesh, India.
E-mail: dr.rojalakshmi@gmail.com

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INTRODUCTION

Odontogenic pathologies encompass a diverse range of conditions, varying from cysts to neoplasms, each with unique biological traits. The most prevalent cysts encountered are radicular cysts, dentigerous cysts (DCs), and odontogenic keratocysts (OKCs), whereas ameloblastomas are the frequently reported benign odontogenic tumours. Dentigerous cysts, known for enclosing immature tooth crowns, distinguish themselves with their delayed growth.[1] OKCs, which originate from the odontogenic epithelium, on the other hand, have a high growth potential and aggression. OKCs are distinguished by their ability to grow to a significant size before clinical detection and their notable tendency to recur following surgical intervention. OKCs underwent nomenclature revisions in the WHO/IARC classification and are now classified as cysts because of insufficient evidence of neoplasms.[2]

Ameloblastomas, deriving from various odontogenic tissues, are benign yet locally aggressive, frequently recurring if not entirely removed.[3] These tumours come in different histopathologic sub-types and variants. Molecular markers aid in understanding these conditions. Glut1, a vital membrane-associated carrier protein omnipresent in tissues, facilitates glucose absorption. Glucose uptake is pivotal for cancer cell growth, making Glut1 a key player.[4] It is involved in cell survival and proliferation, driven by factors such as growth factors, oncogenes, hypoxia, and inflammation. Elevated Glut1 expression is linked to increased glucose uptake, fuelling tumour cell proliferation, local aggressiveness, resistance to therapy, and metastasis, particularly in malignant tumours.[5] It can even inhibit the mitochondrial apoptotic pathway, enhancing cell survival. Despite the existing studies on Glut1, the research on its presence in odontogenic cysts and tumours is limited, resulting in uncertainty regarding its role in these conditions,[6] hence we intend to study the expression of Glut1 in dentigerous cysts, odontogenic keratocysts, and ameloblastoma.

SUBJECTS AND METHODS

This was a retrospective study. Formalin-fixed, paraffin-embedded blocks of histologically confirmed cases of odontogenic keratocysts, dentigerous cysts, multi-cystic ameloblastomas, unicystic ameloblastomas, and dental follicles were retrieved from the archives of the Department of Oral Pathology and Microbiology of GSL DENTAL COLLEGE, Rajahmundry. The sample size was 50 (n = 50), which included 10 cases each of dental follicles, dentigerous cysts, odontogenic keratocysts, multi-cystic ameloblastomas (eight follicular, one acanthomatous, one plexiform variants), and unicystic ameloblastoma. The previously established diagnoses of the selected cases were confirmed using WHO criteria.[7]

Specimens with overt inflammation resulting in the loss of the cystic/lesional epithelium, in most areas of the section, and the improperly stained slides were excluded from the study. Tissue specimen sections from cervical carcinoma were used as positive controls in the study. Negative controls included sections treated identically to the test group, except for omitting the primary antibody. The study received ethical clearance from the Institutional Ethical Committee and was in accordance to the Declaration of Helsinki.

Tissue sections of 4 μm thickness were affixed to Biogenex-coated slides and gently warmed at 58°C for 15 minutes. The paraffin was then removed through a triple xylene treatment, each for 10 minutes, followed by rehydration in graded alcohols, each for 5 minutes. A 10-minute tap water rinse was carried out, and endogenous hydrogen peroxide was neutralized with a 15-minute peroxide block. Antigen retrieval was achieved by immersing the slides in pre-heated trisodium citrate buffer, reheated three times at 600 W for 5 minutes and then cooled to room temperature. Subsequent steps involved washing with PBS and incubating with power block, followed by a 1-hour incubation with the primary antibody (Biogenex) at a 1:100 dilution. After rinsing, a super enhancer was applied, and slides were incubated for 15 minutes. The final steps included incubating with HRP (horse radish peroxide, secondary antibody) for 15 minutes and identifying positive staining as brown under a light microscope using image-capturing software (MICAPS HDM1 camera software).

Quantitative analyses were performed for the sections which were confirmed positive. Two oral pathologists independently observed the cells, and any inter-observer variation was mitigated by calculating the mean values of both observers. Cell counts were performed in three randomly selected representative fields under 200x magnification. The parameters were evaluated as per the adaptation from Furjelova M *et al*.[8]: Percentage of labeled cells: 0: negative, 1: less than 10%, 2: 11 to 50%, 3: greater than 50%. The intensity of staining was scored as follows: 0: no staining, 1: weak (+), 2: moderate (++), 3: strong (+++). Sub-cellular localisation of staining was labelled as (1) nuclear (N) only, (2) cytoplasmic (C) only, (3) membrane (M) only, (4) combined nucleus and cytoplasmic (NC), (5) combined cytoplasmic and

membrane (CM), and (6) combined nucleus, cytoplasmic, and membrane (NCM).

RESULTS

The statistical analysis using the Chi-square test revealed significant insights. In Table 1, it is evident that dental follicles displayed negative staining, while odontogenic keratocysts and unicystic ameloblastomas exhibited a striking presence of labelled cells, with over 50% displaying positive staining, and showed highly significant differences among the groups, with a *P* value of less than 0.001, highlighting the diversity in Glut1 expression levels in the various tissues. In terms of staining intensity, odontogenic keratocysts and unicystic ameloblastomas demonstrated strong staining intensity, suggesting variations in the strength of Glut1 staining in different odontogenic tissues [Table 1]. Finally, the sub-cellular localisation of staining showed significant differences among the groups, with a *P* value of less than 0.05, highlighting variations in the sub-cellular distribution of Glut1 within the tissues.

DISCUSSION

Odontogenic cysts and tumours of the jaws represent a prevalent group of oral-maxillofacial lesions, with around 90% believed to be odontogenic cysts.[9] The epithelium of these cysts originates from various dental structures, including Serres rests, Malassez rests, and a reduced enamel epithelium.[10] Dentigerous cysts, a common non-inflammatory condition, form when fluid accumulates between the enamel epithelium and the tooth crown, often preventing tooth eruption. These cysts are typically asymptomatic and are detected in adolescence or early adulthood, occasionally leading to local growth or infection.[11]

Ameloblastomas, the most common jaw neoplasms, originate from the enamel organ and are usually asymptomatic but possess the potential to become locally aggressive or, rarely, malignant.[12] Identifying the aetiology of odontogenic tumours can be challenging, and immunohistochemistry (IHC) and the analysis of molecular markers have been explored to assist pathologists in their assessment.[13] Some neoplastic cells sustain themselves by exhibiting characteristics such as a high metabolic rate, with glucose serving as a vital energy source. The uptake of glucose is facilitated by a class of transport molecules known as GLUTs, which transport glucose across the cell membrane against its concentration gradient.

Malignant cells, in particular, exhibit high expression of GLUT-1, indicating their elevated glucose demand to fuel rapid cell growth and tumour expansion.[14] GLUT-1 expression is influenced by hormones and metabolic signals. GLUT-1 has also been observed in a few benign head and neck neoplasms, such as ceruminous adenoma and pleomorphic adenoma, suggesting a role in their energy metabolism.[15] Correlations between GLUT-1 expression and 18F-fluorodeoxyglucose (FDG) uptake have been reported in ameloblastomas, reflecting their locally invasive but benign character. In some studies, GLUT-1 has been detected in the membrane and cytoplasm of ameloblastomas.[16]

Even though the presence of Glut 1 is acknowledged by the scientific community, very few studies are present in the literature estimating the Glut1 expression in odontogenic cysts and tumours. Moreover, its role in odontogenic cysts and tumours has remained uncertain. Hence, we intend to study the expression of Glut1 in dentigerous cysts, odontogenic keratocysts, and ameloblastoma.

In the present study, the examination was conducted by two examiners and the kappa value was found to be 0.9, indicating that examiners were in agreement when the percentage of labelled cells was measured. This indicates the reliability of the examination process. Our study found that dental follicles showed no Glut1 staining. This can be

Table 1: Distribution of the study samples in relation with percentage of label cells and intensity of staining

Group	Negative	<10%	11-50%	>50%	Chi square value	*P*
Distribution of the study samples in relation with percentage of label cells						
Dental follicle	10	0	0	0	48.622	<0.001**
Dentigerous cysts	4	3	3	0		
odontogenic keratocysts	0	4	2	4		
Solid ameloblastoma	1	8	1	0		
Unicystic ameloblastoma	1	2	5	2		
Distribution of the study samples in relation with intensity of staining						
Dental follicle	10	0	0	0	24.054	<0.02*
Dentigerous cysts	4	0	6	0		
odontogenic keratocysts	0	4	3	3		
Solid ameloblastoma	1	5	3	1		
Unicystic ameloblastoma	1	1	5	3		

*$P<0.05$ statistically significant

attributed to the absence of rapidly proliferating cells in dental follicles.[17] Such findings align with previous research by Kuroki *et al*.,[18] emphasizing that Glut1 expression tends to rise when cells shift towards a proliferative state. Additionally, GLUT1 expression has been linked negatively to glycogen accumulation in neoplastic renal and hepatic tumours as well as oral mucosa.

The study reveals a varying pattern of GLUT-1 expression in the examined odontogenic lesions. The expression of Glut1 in dentigerous cysts is positive in 60% of the specimens and negative for 40% of the cases [Figure 1b]; the results are in contrast to the study by Vasconcelos *et al*.[19] and Bandyopadhyay A *et al*.[6] This variation suggests that there may be heterogeneity within dentigerous cysts, and some cases might exhibit different metabolic behaviours, potentially due to differences in the molecular characteristics or stages of the cysts. In the study by Vasconcelos *et al*.,[19] 15% of the specimens showed <10% of labelled cells, 40% of the specimens displayed 11–50% of labelled cells, and 45% of the specimens showed <50% of labelled cells. In the current study, 30% of the specimens showed <10% of labelled cells and 30% of the specimens displayed 11–50% of labelled cells, whereas in the study of Bandyopadhyay A *et al*.,[6] 13.3% of the specimens displayed 11–50% of labelled cells and 86.7% of the specimens showed <50% of labelled cells. These discrepancies could be due to variations in the patient populations studied as different demographic and clinical characteristics of patients might result in differences in GLUT1 expression.

In contrast to dentigerous cysts, our study detected consistent Glut1 expression in all odontogenic keratocyst specimens. These results align with previous research by Vasconcelos *et al*.,[19] Bandyopadhyay A *et al*.,[6] and Leite RB *et al*.,[20] highlighting Glut1's significant role in glucose absorption in OKCs. In the study by Vasconcelos *et al*.,[19] 75% of the specimens showed <10% of labelled cells, 30% of the specimens displayed 11–50% of labelled cells, and 65% of the specimens showed <50% of labelled cells. In the current study, 40% of the specimens showed <10% of labelled cells, 20% of the specimens displayed 11–50% of labelled cells, and 40% of the specimens showed <50% of labelled cells, whereas in the study by Bandyopadhyay A *et al*.,[6] 60% of the specimens displayed 11–50% of labelled cells and 40% of the specimens showed <50% of labelled cells. In the study by Leite RB *et al*.,[20] positive immunoexpression of GLUT-1 was observed in the epithelial component of all cases. In the study by Pragallapati and Manyam,[21] 83% of the specimens showed positivity for GLUT 1 and 17% of specimens were negative.

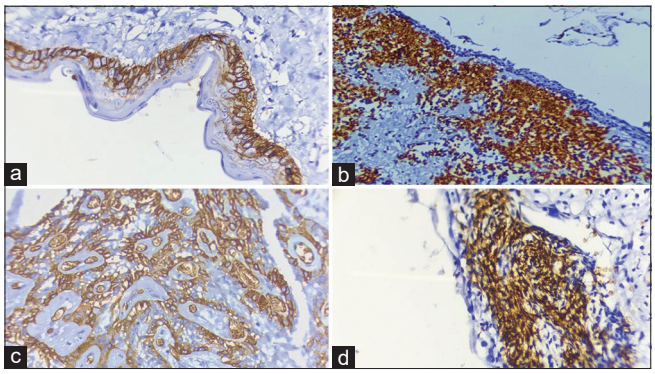

Figure 1: Photomicrograph of GLUT 1 expression: (a) odontogenic keratocysts (x200), (b) dentigerous cysts without staining in the epithelial lining, (c) solid ameloblastoma, (d) and unicystic ameloblastoma (×200)

Expression of Glut1 in ameloblastoma was positive for all the specimens in the study by Vasconcelos *et al*.,[19] Bandyopadhyay A *et al*.,[6] and Sánchez-Romero *et al*.[17] In the current study, 2 specimens out of 20 lacked GLUT1 expression, similar to the study by Pragallapati and Manyam,[21] where 4 specimens turned negative out of 30. In the study by Vasconcelos *et al*.,[19] 15% of the specimens showed <10% of labelled cells, 35% of the specimens displayed 11–50% of labelled cells, and 50% of the specimens showed <50% of labelled cells. In the current study, 50% of the specimens showed <10% of labelled cells, 30% of the specimens displayed 11–50% of labelled cells, and 10% of the specimens showed <50% of labelled cells, whereas in the study of Bandyopadhyay A *et al*.,[6] 73.3% of the specimens displayed 11–50% of labelled cells and 26.6% of the specimens showed <50% of labelled cells. In the study by Pragallapati and Manyam,[21] 10% of the specimens showed <10% of labelled cells, 70% of the specimens displayed 11–50% of labelled cells, and 6% of the specimens showed <50% of labelled cells. Despite minor variations in the percentages of labelled cells, the positive expression of Glut1 in ameloblastoma remains a consistent finding. The small instances of negative expression could be attributed to individual variations or specific sub-types of ameloblastoma.

In the current study, ameloblastomas were further categorised as multi-cystic ameloblastomas and unicystic ameloblastoma. In multi-cystic ameloblastomas, 80% of the specimens showed <10% of labelled cells and 10% of the specimens displayed 11–50% of labelled cells, whereas in unicystic variants, 20% of the specimens showed <10% of labelled cells, 50% of the specimens displayed 11–50% of labelled cells, and 20% of the specimens showed <50% of labelled cells. These results suggest that there may be differences in Glut1 expression between multi-cystic and unicystic ameloblastoma variants. Multi-cystic ameloblastomas tend

to exhibit lower Glut1 expression, with the majority of specimens having less than 10% labelled cells. In contrast, unicystic ameloblastomas show a more variable pattern, with some specimens displaying moderate expression and others showing lower expression levels.

The current study displaces the highest number of labelled cells of >50%, which was observed in odontogenic keratocysts. This is followed by unicystic ameloblastoma in which two specimens displayed labelled cells >50%. Solid ameloblastoma displayed a higher number of specimens in which <10% of labelled cells was observed. A higher number of specimens which displayed 11–50% of labelled cells was observed in unicystic ameloblastoma. In the overall study, the majority of the sample displayed the staining of <10% of cells. Out of all the samples, six specimens displayed >50% of the labelled cells. This was found to be statistically highly significant with a *P* value less than 0.001. These findings suggest that Glut1 expression patterns may be associated with the type and characteristics of odontogenic cysts and tumours. The variations in Glut1 expression can have implications for understanding the metabolic activities and growth patterns of these lesions, potentially offering insights into their pathogenesis and clinical behaviour. The results are in line with the studies conducted by Vasconcelos *et al*.[19] and Bandyopadhyay A *et al*.,[6] where OKC showed >50% labelled cells, followed by ameloblastoma and dentigerous cysts. In the study by Pragallapati and Manyam[21] in 2022, assessment of GLUT1 expression in ameloblastoma and OKC was done. In that investigation, similar to the present study, OKC showed >50% labelled cells, followed by ameloblastoma. These findings indicate that GLUT-1 is over-expressed in the lesions that use the anaerobic glycolytic pathway as a source of growth energy. Vera-Sirera *et al*.[22] observed that OKC had increased GLUT-1 expression when compared to orthokeratinised odontogenic cysts. This suggested that the strong cellular proliferation observed in a variety of different tumour forms may be able to explain the elevated expression of GLUT-1 in OKC.

Staining distribution in dentigerous cysts, OKC, and ameloblastoma was observed. Most specimens had diffuse expression, with a small number of ameloblastoma and OKC cases exhibiting a focused expression pattern. DC and unicystic ameloblastoma specimens exhibited a diffuse expression pattern. However, the distribution pattern appeared to be non-specific in terms of its appearance both in OKC and within the solid ameloblastoma. In OKCs, cells in the basal regions expressed positively [Figure 1a]. In solid ameloblastoma instances, GLUT-1 expression was restricted to central cells and peripheral palisading cells, with no expression in the intermediate region [Figure 1c]. The distribution pattern was similar to the study conducted by Bandyopadhyay A *et al*.[6] GLUT1 immunostaining, however, predominated in deeper layers of the epithelial component of all OKCs tested in the current investigation, and immunoreactivity to these proteins tended to be lacking in cells of the surface layers. The higher demand for glucose absorption by metabolically active cells seen in deeper levels of the epithelial component of these tumours may be the cause of this pattern of GLUT expression in OKCs. In this regard, one of the factors contributing to the potential aggressiveness of these tumours may be the predominance of GLUT-1 mainly in deeper epithelial layers.[21]

The staining intensity ranged from mild to intense among different groups. The staining intensity was moderate in all the immunostained specimens of dentigerous cysts in the current study, whereas in the study by Vasconcelos *et al*.,[19]. 45% showed intense and 40% showed moderate staining. In the present study, 60% of the dentigerous cysts showed moderate and the rest 40% showed no staining. The current study is in contrast to the study by Bandyopadhyay A *et al*.,[6] in which mild staining was noted in 60% of cases, severe staining in 40% of the cases, and no moderate staining was observed in specimens.

The results of the OKC staining intensity varied from mild to intense. The results of current study are in line with the study by Pragallapati and Manyam.[21] Staining intensity in their study varied from mild to intense with intense (23%), mild (60%), and no staining (17%), which is contrast to the present study in which OKC specimens displayed 40% mild, 30% moderate, and 30% intense staining intensity. In the study by Vasconcelos *et al*.,[19] OKC staining intensity varied from mild to intense with intense (40%), moderate (25%), and mild (35%), and in the study by Bandyopadhyay A *et al*.,[6] it was 53.3% intense, 33.3% moderate, and 13.3% mild, which were in contrast to the current study.

The staining intensity of Glut1 immunostaining in ameloblastoma was 20% intense, 40% moderate, 30% mild, and 10% negative for the specimens. In the study by Pragallapati and Manyam,[21] immunostaining was 23.4% intense, 63.3% mild and 13.3% of cases exhibited no staining. The present study is in line with the study by Bandyopadhyay A *et al*.,[6] in which 53.3% of showed mild staining intensity, 33.3% showed moderate, and 13.3% of the cases showed intense staining intensity. The current study is in contrast to Vasconcelos *et al*.,[19] where the specimens displayed 35% mild, 20% moderate, and 45% intense staining intensity.

Among the unicystic and solid ameloblastomas in the present study, the unicystic ameloblastoma exhibited strong intensity when compared to solid ameloblastoma. The small sample size prevents a legitimate discussion of the cause of the low expression, though.

In the present study, strong intensity of staining was observed in odontogenic keratocysts and ameloblastoma. Among the ameloblastomas, three specimens were solid, and three were unicystic ameloblastomas, all of which displayed strong staining [Figure 1d]. Conversely, moderate staining was seen in 17 specimens, including six dentigerous cysts, three odontogenic keratocysts, three solid ameloblastomas, and five unicystic ameloblastomas. Weak staining was observed in 10 specimens, encompassing four odontogenic keratocysts, five solid ameloblastomas, and one unicystic ameloblastoma. Importantly, no staining was observed in dental follicles, four specimens of dentigerous cysts, and two specimens of ameloblastomas (one solid and one unicystic).

The sub-cellular localisation of GLUT1 in the present study was categorised into various patterns, including the nucleus only, cytoplasm only, membrane only, combined cytoplasm and membrane, and combined nucleus, cytoplasm, and membrane. In the present study, sub-cellular localisation in the cytoplasm only was observed in a total of 16 samples. Out of these, three belonged to dentigerous cysts, two belonged to odontogenic keratocysts, five belonged to solid ameloblastoma, and six belonged to unicystic ameloblastoma. In the study by Pragallapati and Manyam,[21] 11 cases of OKC and 12 cases of ameloblastoma showed cytoplasm only staining out of 30 cases. This pattern indicates that in these samples, GLUT1 primarily localises to the cytoplasm of the cells.

In the current study, sub-cellular localisation of membrane only was observed in a total of three samples. Out of these, two were odontogenic keratocysts and one was solid ameloblastoma. In the study by Bandyopadhyay A *et al*.,[6] out of 15 cases of DC, OKC, and ameloblastoma, 2 OKC, 9 DC, and 11 ameloblastoma cases exhibited sub-cellular in membrane only. In the study by Vasconcelos *et al*.,[19] 3 DC, 11 OKC, and 11 ameloblastoma out of 20 cases each exhibited membrane only sub-cellular localisation of Glut 1.

Sub-cellular localisation in the combined cytoplasm and membrane was observed in 15 specimens. Out of these, three were observed in dentigerous cysts, six were observed in odontogenic keratocysts, three were observed in solid ameloblastoma, and three in unicystic ameloblastoma. The results are in line with the study by Pragallapati and Manyam.[21] Ten cases of OKC and 14 cases of ameloblastoma showed combined cytoplasm and membrane staining out of 30 cases. In the study by Bandyopadhyay A *et al*.,[6] out of 15 cases of DC, OKC, and ameloblastoma, 13 OKC, 6 DC, and 4 ameloblastoma cases exhibited sub-cellular localisation in combined cytoplasm and membrane. In the study by Vasconcelos *et al*.,[19] 17 DC, 9 OKC, and 9 ameloblastoma out of 20 cases each exhibited combined cytoplasm and membrane sub-cellular localisation of Glut 1.

The current study's findings align with the existing understanding that the localisation of GLUT1 within a cell can be influenced by various stimuli and conditions, such as growth factors, hypoglycaemia, and hypoxia. These factors play a role in determining the cellular distribution of GLUT1, including whether it is localised in the cell membrane, cytoplasm, or both. In the current study, the three types of staining patterns (membrane only, cytoplasm only, and both membrane and cytoplasm) were observed in all instances, indicating that the localisation of GLUT1 can vary within cells of the same type. This observation is consistent with the study by Pragallapati and Manyam,[21] further supporting the idea that the distribution of GLUT1 can be variable even within similar lesions or cell types. The co-localisation of GLUT1, particularly in the cell membrane and cytoplasm, was more prevalent in OKCs in the current study, followed by ameloblastomas and dentigerous cysts. This suggests that these lesions exhibit increased co-localisation of GLUT1 in these cellular compartments, potentially indicating higher glucose transport activity.

The concept of "unmasking" of the protein, as observed in the initial stages of increased glucose demand, is in line with the study's findings and the broader understanding of GLUT1 regulation. This "unmasking" process enhances GLUT1's affinity for glucose, reflecting the cell's increased glucose transport needs. Further, the study suggests that ongoing stimulation, such as hypoxia or other factors, can lead to the translocation of existing glucose transporters from cytoplasmic vesicles to the plasma membrane, ultimately resulting in an increase in the synthesis of GLUT-1 mRNA.[23] This is an important process that allows cells to adapt to changing metabolic demands.

The role of hypoxia in the expression and localisation of GLUT-1 is further supported by the study's reference to Airley *et al*.,[24] who associated cytoplasmic and membranous expression of GLUT-1 in tumours with the duration and extent of hypoxia in different areas. Co-localisation of GLUT-1 with the Golgi apparatus is suggested to lead to the combined membrane and cytoplasmic expression. These findings provide valuable insights into the mechanisms

that regulate GLUT1 expression and localisation in various pathological conditions, shedding light on the potential relationship between GLUT1 expression patterns and the underlying metabolic and growth characteristics of different lesions.

The limitations of the current study are we did not assess the clinical characteristics of our patients and we could not determine whether the smaller number of GLUT1-expressing samples was due to variations in disease status and development. Changes in GLUT-1 expression and rates of glucose transport are affected by growth rates and oxygen supply. Also, several compounds have been reported to regulate glucose transporter expressions such as hypoxia, estradiol and epidermal growth factor, post-transcriptional regulatory factors, GLUT-1 polymorphisms, and epigenetic events.

CONCLUSION

The process of glucose absorption can be considered the bottleneck in the development and metabolism of cancer cells. Understanding the molecular mechanisms underlying glucose transport is crucial as it serves as the foundation for the rational design of drugs aimed at inhibiting glucose uptake, ultimately arresting tumour growth. The findings of the current study imply that GLUT-1 plays a role in the glucose metabolism of odontogenic cysts and tumours and appears to influence the development of ameloblastomas, odontogenic keratocysts, and dentigerous cysts. This partly explains the variations in the biological behaviour of these lesions. GLUT-1 holds potential as a target for future therapeutic approaches for odontogenic cysts and tumours.

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Conflicts of interest
There are no conflicts of interest.

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