Objectives The aim of this study was to determine the prevalence and clinical features of pigmented oral lesions from Thailand.

Materials and Methods Biopsy records of the Department of Oral Pathology, Chulalongkorn University, Department of Oral Diagnosis, Khon Kaen University, Department of Oral Biology and Oral Diagnostic Sciences, Chiang Mai University, Department of Stomatology, Prince of Songkla University, and Rangsit University were reviewed for oral pigmented lesions diagnosed during 1999 to 2019. Demographic data were culled from the biopsy records. Ages of the patients were subdivided into 10-year intervals. Locations of the lesions were classified as gingiva, labial/buccal mucosa, palate, floor of the mouth, tongue, as well as the combination of sites. Data were analyzed by descriptive statistics using SPSS version 20.0.

Results Of the 47,175 accessioned cases, 241 cases (0.51%) were diagnosed in the category of pigmented oral lesions. The age of the patients ranged from 1 month to 88 years with the mean ± standard deviation = 38.74 ± 20.96 years. Regarding gender, 172 patients (71.37%) with pigmented lesions were females, while 69 patients (28.63%) were males. The female-to-male ratio was 2.49:1. The majority of the pigmented lesions were encountered at the gingiva (29.88%) followed by labial/buccal mucosa (26.97%), palate (14.94%), lip (10.79%), alveolar mucosa (9.54%), and others (7.88%), respectively. The three most common pigmented oral lesions in the present study were nevus (39.83%), followed by melanotic macule (28.63%) and amalgam tattoo (17.43%), respectively.

Conclusions The most common pigmented oral lesion in the present study is nevus. Demographic data of the patients in the present study are in accordance with previous
Introducción

La coloración de la mucosa oral varía desde el rosa hasta el rojo para elgente de piel clara a púrpura en personas con piel de color moreno a negro, dependiendo del grado de queratinización, grosor, vascularización y número de melanocitos, melanocitosis activos así como el tipo de tejido submucoso.1,2 La pigmentación oral puede ser el resultado de un cambio físico o patológico. Las condiciones patológicas pueden clasificarse como endógenas o exógenas dependiendo de la causa. El pigmentación endógena es la que varía de la melanocitosis macule, melanocitosis nevoidea, nevo que presenta inflamación, la pigmentación causada por la deposición directa en el tejido o endógena de pigmentación.2,3 La pigmentación oral también puede clasificarse de acuerdo con la presentación clínica como focal o solitaria.4

Los estudios previos en general son limitados. La mayoría de los estudios anteriores se basan en una sola entidad.4,5 A nuestro conocimiento, no se han realizado solamente dos estudios4,6 sobre pigmentación oral en los centros de diagnóstico oral. En este estudio, se realizaron la prevalencia y las características clínica y patológica de los pacientes con pigmentación oral en el país.

Material y Métodos

Los registros de biopsia del Departamento de Patología Oral; Chulalongkorn University, Departamento de Diagnóstico Oral; Chiangmai University, Departamento de estomatología; Prince of Songkla University y el Departamento de Diagnóstico Oral; Rangsit University fueron revisados para identificar biopsias de pigmentación oral diagnosticadas entre 1999 y 2019. Los datos demográficos fueron extraídos de los registros de biopsia. Las edades de los pacientes fueron subdivididas en intervalos de 10 años. Las ubicaciones de las lesiones se clasificaron como gingiva, labial/buccal mucosa, paladar, interior de la boca, lengua, así como la combinación de sitios. El color de la pigmentación se definió como la vermelización de la parte del labio (labio corporal). Los datos fueron analizados por el software SPSS versión 20.0.

Resultados

De las 47,175 biopsias enlistadas, 241 casos (0,51%) fueron diagnosticados como lesiones pigmentadas de la boca. La prevalencia ranged from 0,32% de Chulalongkorn University en el centro de Tailandia a 1,35% de KhonKaen University en el noreste de Tailandia. La edad de los pacientes varió de 1 mes hasta 88 años con un valor medio ± desviación estándar de 38,74 ± 20,96 años. La mayoría de los pacientes (62,24%) se desarrollaron en la tercera a sexta década de la vida. Sesenta y siete casos (7,05%) fueron diagnosticados en niños menores a 16 años. En el grupo de la tercera a la sexta década de la vida, fueron diagnosticados en niños menores a 16 años, en el grupo de edad de 65 años y mayores. La media de edad del paciente pediátrico fue 11,76 años, mientras que la media del paciente geriátrico fue 71,93 años.

En cuanto al género, 172 pacientes (71,37%) con lesiones pigmentadas fueron mujeres, mientras que 69 pacientes (28,63%) con lesiones pigmentadas fueron hombres. El cociente de la mujer al varón fue 2,49:1. Todas las instituciones participantes mostraron un mayor número de pacientes mujeres que varones. En los grupos pediátrico y geriátrico, también se observó una tendencia femenina. Se observó un mayor número de pacientes mujeres que varones en ambos grupos.

En el grupo de edades más jóvenes, la mayor prevalencia de las lesiones pigmentadas se encontró en la mucosa bucal y gingival (29,88%) seguido por labial/buccal mucosa (26,97%); paladar (14,94%); labio (10,79%) y muco alveolar (9,54%), respectivamente. En los pacientes pediátricos, la mayor frecuencia de lesiones pigmentadas se encontró en la mucosa bucal y gingival (47,06%) seguido por labio (23,53%); en los pacientes geriátricos, la mayor frecuencia de lesiones pigmentadas se encontró en la mucosa bucal y gingival (52,94%); seguido de mucosa bucal y gingival (47,06%) seguido por labio (23,53%).

El nevo fue la lesión pigmentada más prevalente en la mucosa bucal (39,83%) seguido de melanocitosis macule (28,63%) y tatuaje de amalgama (17,43%), respectivamente. Los histogramas de las características clínica y patológica de las lesiones pigmentadas se muestran en Figura 1. Dentro del grupo de nevos, la nevoidea intramucosa fue la lesión más común en pacientes pediátricos (47,06%), seguida de nevoidea intramucosa (47,06%) seguido de pigmentado oral (25,00%); y gingiva (21,43%) seguido por paladar (20,96%)

Nevus was the most prevalent pigmented oral lesion (39.83%) followed by the melanotic macule (26.63%) and amalgam tattoo (17.43%), respectively. The clinicopathological features oral pigmented lesions are shown in Fig. 1. Within the nevus group, intramucosal nevus was the most common lesion accounting for 66.67% of all nevi, followed by compound nevus (25.00% of all nevi) and blue nevus (8.33% of all nevi), respectively. Table 1 shows the clinicopathological features of the patients with pigmented oral lesions in the study. In the pediatric patients aged 16 years and younger, the most common pigmented lesion was compound nevus (52.94% of the pediatric patients), followed by intramucosal nevus (23.53% of the pediatric patients), and melanocytic macule (11.76% of the pediatric patients), respectively. In the elderly patients aged 65 years and older, the most common pigmented lesion was melanocytic macule (35.71% of the elderly patients), followed by amalgam tattoo and melanoma (25.00% of the elderly patients each).

Discusión

Lesiones pigmentadas pueden ser de tipo físico y patológico; algunos de ellos están asociados con trastornos estéticos,7 mientras que algunos de ellos pueden ser peligrosos.8 Los pigmentados
oral lesions in the present study constituted 0.51% of all biopsy cases from Thailand during the 20-year study period that is comparable to 0.07% by Ferreira et al, 0.83% by Buchner et al, 0.90% by Buchner et al, 1.34% by Tavares et al, 5.70% by De Giorgi et al, but lower than 13.50% by Amir et al, and 30.30% by Hassona et al. The explanation for the high prevalence of pigmented oral lesions in the study by Hassona et al is accounted for by the fact that their study is a clinical study and the four most common pigmented lesions are racial pigmentation, smokers’ melanosis, amalgam tattoo, and melanocytic macule. These types of lesions are usually diagnosed in the clinic and are not submitted for histopathological examination. Likewise, the study by Amir et al focused exclusively on physiologic pigmentation in Israeli children, thus demonstrating a relatively high prevalence. Mean age of the patients with pigmented oral lesions in the present study (38.74 years) is comparable to 32.00 years by Buchner et al, 36.60 years by Ferreira et al, 39.00 years by De Giorgi et al, 41.3 years by Hassona et al, 43.70 years by Buchner et al, and 45.00 years by Tavares et al. The majority of pigmented oral lesions in the present study were encountered in females (71.37%) that are in accordance with the study by De Giorgi et al, Buchner et al, Ferreira et al, Tavares et al, and Hassona et al. Certain pathologic entities in which the number of samples was high enough to draw a meaningful conclusion such as nevus, melanotic macule, and amalgam tattoo elicited a two- to threefold F:M ratio.

The three most common pigmented oral lesions in the present study were nevus (39.83%), followed by melanotic macule (28.63%) and amalgam tattoo (17.43%) that are similar to previous stories despite the difference in order and slight pathological entity difference.

Nevi can present as a macule or a papule with pigmentation. It represents the most frequent pigmented oral lesion in the present study accounting for 0.20% of all accessioned

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number (%)</th>
<th>Mean age ± SD</th>
<th>F:M ratio</th>
<th>Most common location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nevus</td>
<td>96 (39.83%)</td>
<td>29.80 ± 17.91</td>
<td>2.20:1</td>
<td>Labial/buccal mucosa (41.67%)</td>
</tr>
<tr>
<td>–Intramucosal nevus</td>
<td>64 (26.56%)</td>
<td>30.81 ± 17.58</td>
<td>2.76:1</td>
<td>Labial/buccal mucosa (51.56%)</td>
</tr>
<tr>
<td>–Compound nevus</td>
<td>24 (9.96%)</td>
<td>26.33 ± 19.87</td>
<td>1.66:1</td>
<td>Lip (20.83%)</td>
</tr>
<tr>
<td>–Blue nevus</td>
<td>8 (3.31%)</td>
<td>32.13 ± 14.78</td>
<td>1.66:1</td>
<td>Palate (50%)</td>
</tr>
<tr>
<td>Melanotic macule</td>
<td>69 (28.63%)</td>
<td>40.83 ± 20.42</td>
<td>3.06:1</td>
<td>Gingiva (33.33%)</td>
</tr>
<tr>
<td>Amalgam tattoo</td>
<td>42 (17.43%)</td>
<td>45.02 ± 22.42</td>
<td>2.82:1</td>
<td>Gingiva (38.10%)</td>
</tr>
<tr>
<td>Melanoma</td>
<td>22 (9.13%)</td>
<td>56.18 ± 16.39</td>
<td>1.44:1</td>
<td>Gingiva (45.45%)</td>
</tr>
<tr>
<td>Physiologic pigmentation</td>
<td>5 (2.07%)</td>
<td>57.00 ± 9.27</td>
<td>4:1</td>
<td>Labial/buccal mucosa (50.00%) and gingiva (50.00%)</td>
</tr>
<tr>
<td>Smoker’s melanosis</td>
<td>5 (2.07%)</td>
<td>41.00 ± 16.73</td>
<td>4:1</td>
<td>Gingiva (100.00%)</td>
</tr>
<tr>
<td>Drug-induced mucosal pigmentation</td>
<td>2 (0.84%)</td>
<td>24.50 ± 23.34</td>
<td>100:1</td>
<td>Labial/buccal mucosa (50.00%) and palate (50.00%)</td>
</tr>
<tr>
<td>Total</td>
<td>241 (100%)</td>
<td>38.74 ± 20.96</td>
<td>2.49:1</td>
<td>Gingiva (29.88%)</td>
</tr>
</tbody>
</table>

Abbreviation: SD, standard deviation.
cases and 39.83% of all pigmented cases that are comparable to 0.06% of all the accessioned cases by Ferreira et al.⁸ and 0.10% of all the accessioned cases by Buchner et al.⁴ but higher than 9.90% by De Giorgi et al.¹¹ 11.80% of by Buchner et al.¹⁰ 20.50% of all pigmented lesions by Tavares et al.³ Mean age of the patients with nevi in the present study was 29.80 years that is comparable to 30.50 years by Buchner et al.,⁴ 32.00 years by Buchner et al.¹⁰ and 36.60 years by Ferreira et al.⁵ Nevi afflicted females more than males as in the previous studies.³,⁴,⁹,¹⁰,¹³ The predilection site for nevi in the present study was labial/buccal mucosa (41.7%) followed by gingiva and palate (17.70% each). This is different from most previous studies⁴,⁹,¹⁰,¹³ which consistently revealed that palate was the predilection site for nevi. This difference may be attributed to the racial difference since most of the patients from previous studies were Caucasians or Blacks, while all the patients in the present study were Asians. Intramucosal nevus constituted the most common histologic subtype of nevus in the present study (66.67%) that is in accordance with previous studies.³,⁴,⁹,¹⁰,¹³ The second most frequent histologic subtype of nevus in the present study was compound nevus (25.03%) followed by blue nevus (8.33%). No junctional nevi were found in the study as reported by Buchner et al that this entity is very rare in oral cavity.¹⁰ Previous studies⁴,⁹,¹⁰,¹³ reported blue nevus was the second most common histologic subtype of nevus followed by compound nevus, while the study by Buchner et al.⁴ showed an equal distribution between compound nevus and blue nevus.

Melanotic macule is a small well-circumscribed brown-to-black macule that occurs on the lip and oral mucosa. Lip lesion is referred to as labial melanotic macule, while those on other parts of the oral mucosa are referred to as oral melanotic macule.⁴,¹⁴ Melanotic macule in the present study accounted for 28.63% of all pigmented oral lesions that is in accordance with 22.90% by Tavares et al.³ but lower than 58.30% by Pennacchiotti et al.,¹² and 86.10% by Buchner et al.,⁴ but higher than 5.70% by Hassona et al.,¹ and 13.30% by De Giorgi et al.¹¹ Mean age of the patients with melanotic macule in the present study was 40.83 years that is comparable to 37.00 years by De Giorgi et al.¹¹ 43.70 years by Buchner et al.,⁴ but higher than 8.90 years by Pennacchiotti et al.¹² The reason why mean age of melanotic macule patients in the study by Pennacchiotti et al.¹² is low is because that study was performed on Latin American children. Mean age of the patients with labial melanotic macule in the present study was 28.19 years, while that of the patients with oral melanotic macule in the present study was 44.74 years. It is noteworthy that the mean age of the oral melanotic macule patients is higher than that of the labial melanotic macule patients. The plausible explanation for this is that lip lesion is more noticeable by both the patient and the clinician than its oral counterpart. Both labial melanotic macule and oral melanotic macule elicited a female predominance that is in accordance with previous studies.¹,³,⁴,¹³ The present study along with previous studies³,⁴,¹²,¹⁵ reported that oral melanotic macule outnum-bered labial melanotic macule except the study by Hassona et al.¹³ that reported the lower vermillion as the most predilection site (82.00%) and the study by De Giorgi et al.¹⁷ that showed an equal distribution between oral melanotic macule and labial melanotic macule.

Amalgam tattoo is a dark gray or blue pigmented macular lesion from traumatic implantation of amalgam into the soft tissues. It was the third most common lesion in the present study comprising 0.09% of all accessioned cases and 17.43% of pigmented oral lesions that are comparable to 0.06% of all accessioned cases by Tavares et al.³ Mean age of the patients with amalgam tattoo in the present was 45.02 years that is in accordance with the study by Buchner and Hansen (43.10 years).¹⁶ Amalgam tattoo showed the female predominance as in previous studies¹²,¹⁶,¹⁷ and was preferentially encountered at gingiva (38.10%) and alveolar mucosa (33.33%) as in previous studies,¹² but different from the study in Brazil that revealed buccal mucosa as the site of predilection.¹⁷

Melanoma is a cancer of pigment-producing cells, melanocytes. Clinical appearance of melanoma can be varied from patch, nodule, or even macule in the oral cavity.⁸ The clinical evaluation of the symmetry, border, color change, and size of oral pigmented lesion is important for clinical diagnosis of melanoma.¹⁸ In this study, it was the fourth most common lesion in the present study accounting for 0.05% of all accessioned cases and 9.13% of all pigmented oral lesions. The number of melanoma cases in this study is quite high. This is accounted for by the fact that this study is a multicenter study from 5 out of 7 major oral pathology biopsy service centers distributed in every corner of Thailand over a 20-year period so we get referral cases especially difficult and malignant cases. Pour et al found 17 melanoma cases in the face area out of 31,181 biopsy or autopsy cases in the northern part of Thailand during the 10-year study period.¹⁹ Dhanuthai et al reported 10 melanoma cases from the oral cavity during 2005 to 2014 from Thailand.²⁰ Mean age of the patients with melanoma in the present study was 56.18 years that is in accordance with previous studies,³,⁴,²¹,²² but lower than 66.7 years by Smith et al.²³ Some studies³,¹²,²³ including the present one showed a slight female predominance, while others revealed the opposite.⁴,²¹,²² The present study revealed that gingiva was the most common site for melanoma (45.45%) followed by palate (31.82%) that is consistent with previous studies⁴,¹⁷,¹⁹ that listed palate as the most common site for melanoma followed by gingiva despite in reverse order or an equal distribution between palate and gingiva.²¹

**Conclusions**

The most common pigmented oral lesion in the present study is oral nevus followed by melanotic macule and amalgam tattoo. Demographic data of the patients in the present study are in accordance with previous studies with only minor differences. Pigmented lesions of the oral cavity may constitute a small portion of the oral pathology biopsies but accurate pathological diagnosis is important since there is an overlap in clinical appearance of benign pigmented lesions and melanoma. Therefore, when in doubt, biopsy must be done to reveal the accurate diagnosis of these group of lesions.
Ethical Approval
The study was performed after approval was received from the Institutional Review Board of the Faculty of Dentistry, Chulalongkorn University.

Conflict of Interest
None declared.

References