

## The Relationship Between Menstrual Cycle and Recurrent Aphthous Stomatitis among Female Students of the Faculty of Dentistry, Syiah Kuala University

### Hubungan antara Siklus Menstruasi dan Stomatitis Aftosa Rekuren pada Mahasiswi Fakultas Kedokteran Gigi Universitas Syiah Kuala

Sarinah Rambe<sup>1</sup>, Liza Meutia Sari<sup>1</sup>, Munifah Abdat<sup>2</sup>, Indah Salsabila<sup>3</sup>

<sup>1</sup> Department of Oral Medicine, Faculty of Dentistry, Universitas Syiah Kuala

<sup>2</sup> Department of Dental Public Health, Faculty of Dentistry, Universitas Syiah Kuala

<sup>3</sup> Dental Student, Faculty of Dentistry, Universitas Syiah Kuala

Correspondence email to: sarinahrambe@usk.ac.id

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#### ABSTRACT

Recurrent aphthous stomatitis (RAS) is a painful oral mucosal disorder that affects many people. It is recurrent and appears during childhood or adolescence. Its pathogenesis is characterized by changes in cellular immune response, may explain how the role of sex hormones function during the menstrual cycle. This study aims to investigate the relationship between RAS and the menstrual cycle. The samples were taken from female students of the Faculty of Dentistry, Syiah Kuala University, with a total sample of 191 students who has experienced RAS or had a history of RAS in the past month. This study consisted of two sections of questions, one about the history of RAS and another about the day of menstruation when RAS occurred. The questions were closed-ended, with yes or no answer options. The data were collected using Google Forms. This study showed that 72.8% of subjects were in the luteal phase and 27.2% of subjects were in the follicular phase. Data analysis used the Chi-Square test ( $p < 0.05$ ) as a significant reference. The results of the statistical test showed  $p = 0.01$ ,  $CI = 1.22-4.93$ ,  $OR = 2.45$ . This showed a significant relationship between the luteal phase of menstruation and RAS. The luteal phase of menstruation had a 2.45 times greater risk of experiencing RAS.

**Keywords:** Recurrent aphthous stomatitis, menstrual cycle, luteal phase, follicular phase

#### ABSTRAK

Stomatitis aftosa rekuren (SAR) merupakan kelainan mukosa oral, nyeri dan menyerang banyak orang. Penyakit ini bersifat rekuren dan muncul pada masa kanak-kanak atau remaja. Patogenesisnya ditandai dengan perubahan respons imun seluler. Perubahan imunologi ini dapat menjelaskan fungsi hormon seks selama siklus menstruasi. Penelitian ini bertujuan untuk mengetahui hubungan antara SAR dan siklus menstruasi. Sampel diambil dari mahasiswi Fakultas Kedokteran Gigi Universitas Syiah Kuala (FKG USK). Total sampel sebanyak 191 mahasiswi yang mengalami SAR atau memiliki riwayat SAR dalam satu bulan terakhir. Penelitian ini terdiri dari dua bagian pertanyaan tentang riwayat SAR dan hari menstruasi saat SAR terjadi. Pertanyaan bersifat tertutup, dengan pilihan jawaban ya atau tidak. Data dikumpulkan menggunakan Google Forms. Penelitian ini menunjukkan bahwa 72,8% subjek berada pada fase luteal dan 27,2% subjek berada pada fase folikular. Analisis data menggunakan uji Chi-Square ( $p < 0,05$ ) sebagai acuan signifikan. Hasil uji statistik menunjukkan  $p = 0,01$ ,  $CI = 1,22-4,93$ ,  $OR = 2,45$ . Hal ini menunjukkan adanya hubungan yang signifikan antara fase luteal menstruasi dengan RAS. Fase luteal menstruasi memiliki risiko SAR 2,45 kali lebih besar.

**Kata kunci:** Stomatitis Aftosa Rekuren, Siklus Menstruasi, Fase Luteal, Fase Folikuler

## INTRODUCTION

Recurrent Aphthous Stomatitis (RAS) is the most prevalent ulcerative disease affecting the oral mucosa.<sup>1</sup> The prevalence of RAS in the global population ranges from 5% to 66%.<sup>2</sup> According the National Riskesdas Report in 2018, the prevalence of RAS in Indonesia is 8%, with Aceh province accounting for 7.9%.<sup>3</sup>

The etiology of RAS is unclear at this time, but predisposing factors, including genetics, trauma, stress, viral, and bacterial infections, systemic diseases, hormonal changes (menstrual cycle), hematinic deficiencies (iron, folic acid or vitamin B12), and allergy.<sup>4,5</sup> One of the predisposing factors for inducing RAS is hormonal changes and several researchers have reported a relationship between the menstrual cycle and RAS.<sup>6</sup>

Chiang et al. found that hormonal changes during the luteal menstrual cycle contribute to the emergence of RAS.<sup>7</sup> According to study by Quieros et al., RAS occurred more frequently in women than men. In 68 cases of RAS, the incidence of RAS in men was 40.8%, while in women it was 59.2%, with an average age of 41.9 years.<sup>8</sup>

Balan et al. showed that hormonal changes during puberty, pregnancy, menstruation, and menopause period affect the oral mucosa differently. Oral ulcers, recurrent herpetic lesions, and increased gingival bleeding in women during normal menstrual periods, could be related to hormonal turnover in women during normal menstrual periods.<sup>9</sup> Maheswaran et al. found many variations of time in the appearance of RAS during the menstrual cycle, but the most frequent RAS occurs in the third week, known as the luteal phase.<sup>10</sup> Many studies are interested in determining whether the menstrual cycle and RAS are related or not. These studies showed variation of the results. However, there has been no research examining this issue in Banda Aceh. To the best of our knowledge, this is the first report on the association between RAS and the menstrual cycle that was conducted at Faculty of Dentistry, Syiah Kuala University.

## RESEARCH METHODS

This is a cross-sectional analytic study of 191 subjects. Inclusion criteria: ages range 18-25 years old, willing to be a research

subject, currently experiencing oral ulcers at the time of the study or a history of oral ulcers in the last 3 months, and normal menstrual cycle of 21–30 days. Exclusion criteria: subjects who were pregnant and had autoimmune diseases or other conditions that can impact sex hormones.

The subjects were contacted via cell phone or WhatsApp, then inquired about their willingness to participate in the study. Subjects were asked to answer questions on a google forms consisting of two sections of questions. Section A contains 10 yes and no questions about the history of RAS (presence or absence of menstrual cycle regularity, frequency of occurrence of RAS in a month, the last 3 months, and during menstruation, genetic linkage, trauma, allergies, medical diseases, and drugs). Section B contains 4 “yes” and “no” questions regarding the phase of menstruation when RAS occurs. (1) whether RAS appears during menstruation, (2) 1-7 days before and (3) after menstruation, and (4) whether RAS appears 10 days after menstruation. If most of the “yes” answers are in point 1 and 2, then the subject is included in the follicular phase. If the “yes” answer is mostly in points 3 and 4, then the subject is included in the luteal phase. After completing the form subjects received a brochure via WhatsApp containing information how to reduce the recurrence of RAS lesions.

Univariate analysis was used to describe the data characteristics of each research variable. Bivariate analysis used the Chi-Square test to investigate the relationship between the history of RAS and the menstrual cycle. Data was input using the Statistical Product and Service Solution (SPSS) version 20.0 program.

## RESULTS

This study was conducted for two months on students at the Dentistry Faculty of Universitas Syiah Kuala. Table 1 shows the incidence of RAS in subjects. According to the RAS type, there were 159 (83.24%) subjects who experienced the minor type. The incidence of RAS had the highest frequency of mild, with 156 subjects (81.67%).

Table 1. Distribution of age, menstrual cycle, and recurrent aphthous stomatitis.

| Variable           | Characteristic           | N   | (%)   |
|--------------------|--------------------------|-----|-------|
| Age (y.o)          | 18-21                    | 120 | 62.82 |
|                    | 22-25                    | 71  | 37.17 |
| Menstrual cycle    | Menstrual phase*         | 38  | 19.89 |
|                    | Follicular phase*        | 14  | 7.32  |
|                    | Ovulation phase**        | 37  | 19.37 |
|                    | Luteal phase**           | 102 | 53.40 |
| RAS frequency/year | Mild (< 6 episodes)      | 156 | 81.67 |
|                    | Moderate (6-12 episodes) | 35  | 18.32 |
|                    | Severe (> 12 episodes)   | 0   | 0     |
|                    | RAS type                 |     |       |
|                    | Minor                    | 159 | 83.24 |
|                    | Major                    | 32  | 16.75 |
|                    | Herpetiform              | 0   | 0     |

Menstrual phase: Day 1-5 of menstrual period.  
 Follicular phase: 4-5 to 13 (day 1-14)  
 Ovulation phase: 14 days before menses  
 Luteal phase: The phase begins on day 15 to day 28 after menstrual period  
 \*, \*\*: Merged cells for bivariate statistical analysis (Chi-square test)

Table 2 shows the predisposing factors of RAS in the subjects. This study has several predisposing factors for RAS, such as genetics, hormonal, trauma, allergy, systemic diseases, and drugs.

Table 2. Characteristics of predisposing factors in recurrent aphthous stomatitis.

| Predisposing Factors | Total (n) | Percentage (%) |
|----------------------|-----------|----------------|
| 1                    | 89        | 46,59          |
| 2                    | 80        | 41,88          |
| ≥ 3                  | 22        | 11,51          |

Table 3 showed that 139 subjects (72.80%) experienced RAS in the luteal phase and 52 subjects (27.20%) experienced RAS in the follicular phase.

Table 3. The relationship between the menstrual cycle and recurrent aphthous stomatitis.

| Menstrual phase | RAS |      | CI    | OR   | p           |
|-----------------|-----|------|-------|------|-------------|
|                 | N   | %    |       |      |             |
| Luteal          | 139 | 72,8 | 1,22- | 2,45 | <b>0,01</b> |
| Follicular      | 52  | 27,2 | 4,93  |      |             |

Based on the OR value, the risk of RAS is 2.45 times higher in the luteal phase than in the follicular. This demonstrates that RAS appears more frequently in the luteal phase than in the follicular phase.

**DISCUSSION**

Individuals have different predisposing factors for RAS. In this study, RAS was found at 18-25 years old. The findings of this study are consistent with Usha et al. RAS typically begins at the age of 19 and is most common between the ages of 18 and 24.<sup>11</sup> At a productive age, individuals may experience stress, irregular eating patterns, and hormonal changes, which can lead to the emergence of RAS.<sup>12,13</sup>

Trauma was identified as the most common risk factor for RAS in this study. RAS is not the same as a traumatic ulcer. Trauma from brushing teeth or accidentally biting the oral mucosa can cause this condition.<sup>14,15</sup> Trauma can cause ulcers in RAS patients, these are typically localized and do not affect the masticatory mucosa. Bites, dentures, or chemicals typically cause traumatic ulcers and occur in vulnerable areas like the lips, buccal mucosa, or adjacent dentures.<sup>16</sup>

The genetic factor is a predisposing factor for RAS. The study found that family members shared the subject's experience with RAS. Human Leukocyte Antigen (HLA) shows that parents' involvement can trigger SAR in their children.<sup>5,14</sup>

The menstrual cycle is a natural process in the female reproductive system that occurs monthly from menarche (first menstrual bleeding during puberty) to menopause, allowing for fertility and pregnancy.<sup>17</sup> The average menstrual cycle is 28 days, and the average duration of menstrual flow is 4 to 6 days. The menstrual cycle occurs in two phases that are triggered by ovulation.<sup>18</sup> First, the follicular phase or proliferative phase (during menstruation until ovulation), second the luteal phase or secretory phase (between ovulation and the start of menstruation).<sup>19</sup>

The distribution of women suffering from SAR was based on the menstrual cycle phase, and the data obtained revealed that SAR occurs in the luteal phase. There was a significant difference between the luteal phase and the follicular phase. The follicular phase



begins on the first day of menstruation, in women aged 19 to 42 years, the follicular phase has an average duration of 14.6 days.<sup>7</sup> During the follicular phase, follicle stimulant hormone (FSH) increases up to two days before ovulation.<sup>15</sup> In the middle of the follicular phase, the estrogen increases dramatically. While progesterone remains within normal limits.<sup>15</sup>

Recurrent aphthous stomatitis during menstruation period is caused by a sudden decrease in estrogen and progesterone hormones level. This can happen when fertilization fails, preventing the corpus luteum, which secretes progesterone, from surviving.<sup>6,13</sup> According to Jason and Maso, fluctuating estrogen and progesterone levels affect oral cavity receptors.<sup>20</sup> Estrogen promotes complete maturation of oral mucosal epithelial cells, whereas progesterone inhibits it.<sup>21</sup> Previous studies indicate that the oral mucosa is sensitive to estrogen and progesterone levels during different phases of menstruation.<sup>22,23</sup>

A decrease in estrogen levels can cause epithelium thinning and reducing keratinization of the oral mucosa.<sup>6,9,23</sup> A decreased of estrogen level can cause a decrease in blood flow, which reduces blood supply to the periphery mucosa.<sup>13</sup> A decrease in blood supply to the periphery will cause imbalance problems in epithelial cells, including those in the oral mucosa.<sup>13</sup> Slowness of keratinization process makes the oral mucosa become more sensitive to local irritation and it will increase the risk of RAS.<sup>13</sup> Estrogen is known to control cell growth, differentiation, and function in both reproductive and non-reproductive tissues.<sup>22,24</sup>

Soetiarto and Sumintarti reported that in the mid-luteal phase to the end of the luteal phase, there is a decrease in progesterone level which reducing the self-limiting effect and it can cause the reducing of polymorphonuclear leucocytes and vascular permeability.<sup>21</sup> This increase in permeability of oral mucosa raises levels of inflammatory cytokines, making it easier for bacteria to invade the oral cavity, causing irritation or infection and, eventually, ulcers in the luteal phase.<sup>6,23</sup>

## CONCLUSION

The onset of RAS was found to be more prevalent in the luteal phase among women. Further research is required to determine how much hormone level can contribute to the clinical manifestation of RAS.

## CONFLICT OF INTEREST

We declare no conflict of interest

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