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ORIGINAL ARTICLE

Correlation of Calcium Intake and the Intensity Of Primary Dysmenorrhea in Adolescents

Hubungan Asupan Kalsium dengan Intensitas Dismenore Primer pada Remaja

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ABSTRACT

Background

Primary dysmenorrhea is lower abdominal pain happening during menstruation which is not associated with other diseases or pathology, mostly experienced by adolescents around the world, including in Indonesia. Calcium intake is considered to affect decreasing the intensity of primary dysmenorrhea. Lack of calcium can cause muscle spasms and contractions. However, the average daily intake of calcium in adolescents in Indonesia is still below the recommended adequacy rate. This study aimed to assess the correlation between calcium intake and the intensity of primary dysmenorrhea in adolescents.

Methods

This study was done from March 2019 until January 2020; Analyzed the correlation between calcium intake and intensity of primary dysmenorrhea in 62 adolescents. Calcium intake was assessed using a semi-quantitative food frequency questionnaire, while the power of primary dysmenorrhea was assessed using a Visual Analogue Scale questionnaire.

Results

There were 45.2% of adolescents experienced moderate and severe primary dysmenorrhea. In addition, 51.6% of adolescents experienced less calcium intake, with an average of 804.9 mg per day. The results showed a correlation between calcium intake and the intensity of primary dysmenorrhea ($p = 0.000$).

Conclusions

Calcium intake is related to the intensity of primary dysmenorrhea. While calcium intake in adolescents is still lacking, it is recommended to consume adequate calcium intake.

Keywords: Calcium intake; intensity of primary dysmenorrhea; adolescents

ABSTRAK**Latar Belakang**

Dismenore primer adalah nyeri perut bawah saat haid yang tidak berhubungan dengan penyakit tertentu, sebagian besar dialami oleh remaja di seluruh dunia termasuk Indonesia. Asupan kalsium dinilai berpengaruh terhadap penurunan intensitas dismenore. Kadar kalsium yang kurang dapat menyebabkan spasme dan kontraksi otot. Rerata asupan kalsium per hari pada remaja di Indonesia masih di bawah angka kecukupan kalsium yang dianjurkan. Tujuan penelitian ini adalah menilai hubungan antara asupan kalsium dengan intensitas dismenore primer pada remaja.

Metode

Penelitian ini dilakukan pada bulan Maret 2019 sampai dengan Januari 2020; Menganalisis hubungan antara asupan kalsium dengan intensitas dismenore primer pada 62 remaja. Asupan kalsium dinilai menggunakan semi quantitative food frequency questionnaire, sedangkan intensitas dismenore primer dinilai menggunakan visual analogue scale.

Hasil

Terdapat sebesar 45.2% remaja mengalami dismenore primer dengan intensitas sedang dan berat, sebesar 51.6% remaja kurang mengonsumsi asupan kalsium dengan rerata asupan kalsium sebanyak 804.9 mg per hari. Hasil analisis menunjukkan terdapat hubungan antara asupan kalsium dengan intensitas dismenore primer ($p = 0.000$).

Kesimpulan

Terdapat hubungan antara asupan kalsium dengan intensitas dismenore primer. Rerata asupan kalsium pada remaja masih kurang, oleh karena itu dianjurkan untuk mengonsumsi asupan kalsium yang cukup.

Kata Kunci: Asupan kalsium; intensitas dismenore primer; remaja

INTRODUCTION

Primary dysmenorrhea is defined as abdominal pain during menstruation, usually characterized by cramping and centred in the lower abdomen, which is not associated with any particular disease or disorder.¹ Complaints of dysmenorrhea vary from mild to severe intensity. The prevalence of dysmenorrhea in Indonesia is still high at 64.25%, with 54.89% of them being primary dysmenorrhea and 60-75% occurring in adolescents.² Dysmenorrhea can cause limitations in adolescents' daily activities, such as difficulty concentrating on studying, and decreased learning motivation.³ There are several risk factors for dysmenorrhea, one of which is calcium intake.^{4,5}

In a study conducted by Desrida et al. conducted in Agam Regency, West Sumatra, it was found that the average calcium intake in adolescents was below the Recommended Dietary Allowances (RDA), which was only 882.7 mg/day, from what should have been 1200 mg/day.^{6,7} Adolescence is an age that is very concerned about appearance problems. One of the most common problems faced is an improper diet. This causes a lack of intake of foods such as milk, meat, cheese and their processed products, which are the largest sources of calcium.⁸

The results of research conducted by Chandarabi SM-A et al. concluded that the administration of calcium, either with magnesium or not, is effective in reducing the intensity of primary

dysmenorrhea. This is due to the effect of calcium on neuromuscular activity.⁴ The same results were shown by a study conducted by Tih F et al. Based on this study, consumption of calcium supplements can reduce the intensity of primary dysmenorrhea and premenstrual syndrome in women aged 19-23 years.⁹ Different results were shown in a study conducted by Zarei S et al. The administration of calcium and vitamin D was not significantly different compared to the placebo in reducing the intensity of dysmenorrhea.¹⁰

Based on the pros and cons of previous studies and the high prevalence of dysmenorrhea, this study was conducted to know the relationship between calcium intake and the intensity of dysmenorrhea in adolescents.

METHODS

This study is an observational analytic study with a cross-sectional design. The study location was at SMP Pelita II Jakarta from March 2019 to January 2020. The sample of this study consisted of 62 active students of class VIII and IX of SMP Pelita II Jakarta who met the inclusion criteria aged 13-15 years, had experienced menstruation and were willing to participate in the study. Exclusion criteria include suffering from diseases that affect dysmenorrhea, such as endometriosis, ovarian cysts, tumours, uterine myomas, cervical stenosis, pelvic inflammatory disease, and pelvic adhesions. The sampling technique was done by simple random sampling. Calcium intake was assessed using a semi-quantitative food frequency questionnaire (SQ-FFQ).^{11,12} Each respondent was guided regarding the list of foods and beverages containing high calcium along with the frequency and amount consumed in household units in the last month. The data was then processed using the Nutrisurvey2007 application to obtain the average daily intake of calcium for each respondent. Assessment of calcium intake is categorized as less if it is below the RDA and good if it is above the RDA. The visual analogue pain scale (VAS) determined the intensity of dysmenorrhea.^{13,14} Data analysis was performed using the SPSS 23.0 program with the Chi-Square test, with a confidence limit ($\alpha=0.05$). This research has received ethical approval from the research ethics committee of the Faculty of Medicine, Universitas Trisakti, with the number 97/KER-FK/VII/2019.

RESULTS

Tabel 1. Characteristics of research subjects

Variable	Frequency (n)	Percentage (%)
Calcium Intake		
Low	32	51.6
Good	30	48.4
Primary Dysmenorrhea Intensity		
No Pain	15	24.2
Mild Pain	19	30.6
Moderate Pain	15	24.2
Severe Pain	13	21.0

Table 1 shows that more than half of the respondents (51.6%) consume less calcium intake. Based on data from the SQ-FFQ questionnaire and processed with the Nutrisurvey application, the average calcium intake of respondents in this study was 804.9 mg per day. There were 75.8% of respondents who experienced primary dysmenorrhea, and more than half of that number, namely 45.2%, had moderate to severe dysmenorrhea.

Table 2. Relationship between calcium intake and primary dysmenorrhea intensity

Variable	Primary Dysmenorrhea Intensity						P value
	No pain		Mild pain		Moderate-severe pain		
	n	%	n	%	n	%	
Calcium intake							
Low	2	6.3	7	21.9	23	71.8	0.000*
Good	13	43.3	12	40	5	16.7	

* Chi-Square test

Of respondents with low calcium intake, 71.9% experienced dysmenorrhea with moderate to severe intensity. In respondents with good calcium intake, the majority did not experience pain or mild pain, and only 16.7% experienced moderate pain. Based on statistical tests, there was a significant relationship between calcium intake and the intensity of primary dysmenorrhea ($p=0.000$).

DISCUSSION

In this study, more than half of the respondents (51.6%) consumed less calcium, with an average intake of 804.9 mg daily. This result is still less than the amount recommended by the Indonesian Nutritional Adequacy Rate, 1200 mg daily.⁷ The results are more or less the same as the research conducted by Desrida et al. The study was conducted on 148 young women in Agam Regency, West Sumatra, who assessed calcium levels using a modified food frequency questionnaire. The average amount of calcium intake was 882.7 mg per day.⁶ The results differed from Safitri et al.'s study, with an average calcium intake of 183 mg/day.¹⁵ The study was conducted on 65 students of class XI SMA Negeri 2 Palu with a food recall questionnaire at 2x24 o'clock. The low average calcium intake was assessed because a food recall questionnaire was less precise than a food frequency questionnaire. In addition, teenagers tend to go on an extreme diet without paying attention to the nutritional content in food, including calcium intake. Research conducted by Hidayati KR et al. in Surakarta showed that the average calcium intake of adolescent girls was 437.7 mg/day.¹⁶ The study was conducted on 67 female students using a semi-quantitative food frequency questionnaire processed with the Nutrisurvey program. This low yield is due to the low consumption of calcium sources due to socioeconomic levels that affect the purchasing power of a variety of well-nourished foods.

As many as 75.8% of respondents experienced dysmenorrhea with mild to severe intensity. The majority experienced mild dysmenorrhea intensity, which is equal to 30.6%. The prevalence of dysmenorrhea obtained in this study is the same as the results of systematic reviews conducted by Ju H et al., with prevalence ranging from 67%-90%.³ Research conducted by Bahri et al. and Hidayati

et al. showed almost the same prevalence of dysmenorrhea, namely 82.3%, with the majority of the intensity of dysmenorrhea being mild and 82.1% with the majority being the moderate intensity of dysmenorrhea. In Bahri et al.'s study, the intensity of dysmenorrhea was assessed based on interviews using a questionnaire measuring instrument conducted on 96 people in West Sumatra.¹⁷ Hidayati et al.'s research was conducted in Surakarta with a total of 67 female respondents. This study assessed the intensity of dysmenorrhea using a universal pain assessment tool.¹⁶ In a study conducted on adolescent girls in Japan, the prevalence of dysmenorrhea was 85%.¹⁸ In this study, the pain sensitivity questionnaire was used, which assessed several factors more than the visual analogue scale used in this study.

This study concluded that there was a relationship between calcium intake and the intensity of primary dysmenorrhea ($p = 0.000$). These results are in accordance with research conducted by Razzak et al. on 127 Jordan University of Science and Technology students aged 19 - 24 years that there is a relationship between intake of dairy products and a decrease in dysmenorrhea complaints ($p=0.000$).⁵ Dairy products themselves are a source of food that is high in calcium content.⁷ Research conducted by Tih F et al. at the University in Bandung City on 60 female students aged 19 - 23 years who experienced symptoms of premenstrual syndrome and dysmenorrhea, it was found that consumption of calcium or magnesium supplements reduced complaints of dysmenorrhea and symptoms of premenstrual syndrome ($p=0.000$).⁹ Calcium affects the permeability of nerve membrane. As a stabilizer, calcium can regulate muscle cells in response to nerve stimuli through various pathways. Decreased levels of calcium in the blood cause muscle spasms and contractions.¹⁹ Muscle contractions that last a long time cause ischemia and hypoxia of the uterine muscles, which ultimately lead to dysmenorrhea.²⁰ In a study conducted by Hidayati KR et al. The results showed that most respondents with low calcium intake felt moderate pain. Respondents with normal calcium intake showed less dysmenorrhea than those with low calcium intake. The study stated that the higher the calcium intake, the less the intensity of dysmenorrhea ($r=-0.415$, $p=0.000$).¹⁶

In this study, calcium intake was measured using a semi-quantitative food frequency questionnaire (SQ-FFQ), which assesses food and beverage intake in the last month so that the accuracy highly depends on the respondent's memory. Further research suggests measuring levels of calcium in the blood so that it can accurately describe the effect of calcium on the intensity of dysmenorrhea. This study did not analyse other factors that influence dysmenorrhea, such as stress, smoking, family history of dysmenorrhea, and intake of vitamin D and magnesium.

CONCLUSION

The prevalence of adolescents with low calcium intake is 51.6%. About 75.8% of respondents experienced primary dysmenorrhea, and 45.2% of them experienced moderate to severe dysmenorrhea. There is a relationship between calcium intake and the intensity of dysmenorrhea. Further research is needed with different methods to explain the causal relationship between calcium intake and the intensity of dysmenorrhea and other variables that affect the intensity of dysmenorrhea.

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AUTHORS CONTRIBUTION

Authors contributed to the manuscript writing, data collection and analysis. AD contributed to the improvement of the script. All authors have read the final manuscript and gave their consent.

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by Arleen Devita

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Correlation of Calcium Intake and the Intensity Of Primary Dysmenorrhea in Adolescents

Hubungan Asupan Kalsium dengan Intensitas Dismenore Primer pada Remaja

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ABSTRACT

Background

Primary dysmenorrhea is lower abdominal pain happening during menstruation which is not associated with other diseases or pathology, mostly experienced by adolescents around the world, including in Indonesia. Calcium intake is considered to affect decreasing the intensity of primary dysmenorrhea. Lack of calcium can cause muscle spasms and contractions. However, the average daily intake of calcium in adolescents in Indonesia is still below the recommended adequacy rate. This study aimed to assess the correlation between calcium intake and the intensity of primary dysmenorrhea in adolescents.

Methods

This study was done from March 2019 until January 2020; Analyzed the correlation between calcium intake and intensity of primary dysmenorrhea in 62 adolescents. Calcium intake was assessed using a semi-quantitative food frequency questionnaire, while the power of primary dysmenorrhea was assessed using a Visual Analogue Scale questionnaire.

Results

There were 45.2% of adolescents experienced moderate and severe primary dysmenorrhea. In addition, 51.6% of adolescents experienced less calcium intake, with an average of 804.9 mg per day. The results showed a correlation between calcium intake and the intensity of primary dysmenorrhea ($p = 0.000$).

Conclusions

Calcium intake is related to the intensity of primary dysmenorrhea. While calcium intake in adolescents is still lacking, it is recommended to consume adequate calcium intake.

Keywords: Calcium intake; intensity of primary dysmenorrhea; adolescents

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ABSTRAK**Latar Belakang**

Dismenore primer adalah nyeri perut bawah saat haid yang tidak berhubungan dengan penyakit tertentu, sebagian besar dialami oleh remaja di seluruh dunia termasuk Indonesia. Asupan kalsium dinilai berpengaruh terhadap penurunan intensitas dismenore. Kadar kalsium yang kurang dapat menyebabkan spasme dan kontraksi otot. Rerata asupan kalsium per hari pada remaja di Indonesia masih di bawah angka kecukupan kalsium yang dianjurkan. Tujuan penelitian ini adalah menilai hubungan antara asupan kalsium dengan intensitas dismenore primer pada remaja.

Metode

Penelitian ini dilakukan pada bulan Maret 2019 sampai dengan Januari 2020; Menganalisis hubungan antara asupan kalsium dengan intensitas dismenore primer pada 62 remaja. Asupan kalsium dinilai menggunakan semi quantitative food frequency questionnaire, sedangkan intensitas dismenore primer dinilai menggunakan visual analogue scale.

Hasil

Terdapat sebesar 45.2% remaja mengalami dismenore primer dengan intensitas sedang dan berat, sebesar 51.6% remaja kurang mengonsumsi asupan kalsium dengan rerata asupan kalsium sebanyak 804.9 mg per hari. Hasil analisis menunjukkan terdapat hubungan antara asupan kalsium dengan intensitas dismenore primer ($p = 0.000$).

Kesimpulan

Terdapat hubungan antara asupan kalsium dengan intensitas dismenore primer. Rerata asupan kalsium pada remaja masih kurang, oleh karena itu dianjurkan untuk mengonsumsi asupan kalsium yang cukup.

Kata Kunci: Asupan kalsium; intensitas dismenore primer; remaja

INTRODUCTION

Primary dysmenorrhea is defined as abdominal pain during menstruation, usually characterized by cramping and centred in the lower abdomen, which is not associated with any particular disease or disorder.¹ Complaints of dysmenorrhea vary from mild to severe intensity. The prevalence of dysmenorrhea in Indonesia is still high at 64.25%, with 54.89% of them being primary dysmenorrhea and 60-75% occurring in adolescents.² Dysmenorrhea can cause limitations in adolescents' daily activities, such as difficulty concentrating on studying, and decreased learning motivation.³ There are several risk factors for dysmenorrhea, one of which is calcium intake.^{4,5}

In a study conducted by Desrida et al. conducted in Agam Regency, West Sumatra, it was found that the average calcium intake in adolescents was below the Recommended Dietary Allowances (RDA), which was only 882.7 mg/day, from what should have been 1200 mg/day.^{6,7} Adolescence is an age that is very concerned about appearance problems. One of the most common problems faced is an improper diet. This causes a lack of intake of foods such as milk, meat, cheese and their processed products, which are the largest sources of calcium.⁸

The results of research conducted by Chandarini SM-A et al. concluded that the administration of calcium, either with magnesium or not, is effective in reducing the intensity of primary

dysmenorrhea. This is due to the effect of calcium on neuromuscular activity.⁴ The same results were shown by a study conducted by Tih F et al.⁵ Based on this study, consumption of calcium supplements can reduce the intensity of primary dysmenorrhea and premenstrual syndrome in women aged 19-23 years.⁹ Different results were shown in a study conducted by Zarei S et al. The administration of calcium and vitamin D was not significantly different compared to the placebo in reducing the intensity of dysmenorrhea.¹⁰

Based on the pros and cons of previous studies and the high prevalence of dysmenorrhea, this study was conducted to know the relationship between calcium intake and the intensity of dysmenorrhea in adolescents.

METHODS

This study is an observational analytic study with a cross-sectional design. The study location was at SMP Pelita II Jakarta from March 2019 to January 2020. The sample of this study consisted of 62 active students of class VIII and IX of SMP Pelita II Jakarta who met the inclusion criteria aged 13-15 years, had experienced menstruation and were willing to participate in the study. Exclusion criteria include suffering from diseases that affect dysmenorrhea, such as endometriosis, ovarian cysts, tumours, uterine myomas, cervical stenosis, pelvic inflammatory disease, and pelvic adhesions. The sampling technique was done by simple random sampling. Calcium intake was assessed using a semi-quantitative food frequency questionnaire (SQ-FFQ).^{11,12} Each respondent was guided regarding the list of foods and beverages containing high calcium along with the frequency and amount consumed in household units in the last month. The data was then processed using the Nutrisurvey2007 application to obtain the average daily intake of calcium for each respondent. Assessment of calcium intake is categorized as less if it is below the RDA and good if it is above the RDA. The visual analogue pain scale (VAS) determined the intensity of dysmenorrhea.^{13,14} Data analysis was performed using the SPSS 25.0 program with the Chi-Square test, with a confidence limit ($\alpha=0.05$). This research has received ethical approval from the research ethics committee of the Faculty of Medicine, Universitas Trisakti, with the number 97/KER-FK/VII/2019.

RESULTS

Tabel 1. Characteristics of research subjects

Variable	Frequency (n)	Percentage (%)
Calcium Intake		
Low	32	51.6
Good	30	48.4
Primary Dysmenorrhea Intensity		
No Pain	15	24.2
Mild Pain	19	30.6
Moderate Pain	15	24.2
Severe Pain	13	21.0

Table 1 shows that more than half of the respondents (51.6%) consume less calcium intake. Based on data from the SQ-FFQ questionnaire and processed with the Nutrisurvey application, the average calcium intake of respondents in this study was 804.9 mg per day. There were 75.8% of respondents who experienced primary dysmenorrhea, and more than half of that number, namely 45.2%, had moderate to severe dysmenorrhea.

Table 2. Relationship between calcium intake and primary dysmenorrhea intensity

Variable	Primary Dysmenorrhea Intensity						P value
	No pain		Mild pain		Moderate-severe pain		
	n	%	n	%	n	%	
Calcium intake							
Low	2	6.3	7	21.9	23	71.8	0.000*
Good	13	43.3	12	40	5	16.7	

* Chi-Square test

Of respondents with low calcium intake, 71.9% experienced dysmenorrhea with moderate to severe intensity. In respondents with good calcium intake, the majority did not experience pain or mild pain, and only 16.7% experienced moderate pain. Based on statistical tests, there was a significant relationship between calcium intake and the intensity of primary dysmenorrhea (p=0.000).

DISCUSSION

In this study, more than half of the respondents (51.6%) consumed less calcium, with an average intake of 804.9 mg daily. This result is still less than the amount recommended by the Indonesian Nutritional Adequacy Rate, 1200 mg daily.⁷ The results are more or less the same as the research conducted by Desrida et al. The study was conducted on 148 young women in Agam Regency, West Sumatra, who assessed calcium levels using a modified food frequency questionnaire. The average amount of calcium intake was 882.7 mg per day.⁶ The results differed from Safitri et al.'s study, with an average calcium intake of 183 mg/day.¹⁵ The study was conducted on 65 students of class XI SMA Negeri 2 Palu with a food recall questionnaire at 2x24 o'clock. The low average calcium intake was assessed because a food recall questionnaire was less precise than a food frequency questionnaire. In addition, teenagers tend to go on an extreme diet without paying attention to the nutritional content in food, including calcium intake. Research conducted by Hidayati KR et al.²⁵ in Surakarta showed that the average calcium intake of adolescent girls was 437.7 mg/day.¹⁶ The study was conducted on 67 female students using a semi-quantitative food frequency questionnaire processed with the Nutrisurvey program. This low yield is due to the low consumption of calcium sources due to socioeconomic levels that affect the purchasing power of a variety of well-nourished foods.

As many as 75.8% of respondents experienced dysmenorrhea with mild to severe intensity. The majority experienced mild dysmenorrhea intensity, which is equal to 30.6%. The prevalence of dysmenorrhea obtained in this study is the same as the results of systematic reviews conducted by Ju H et al., with prevalence ranging from 67%-90%.³ Research conducted by Bahri et al. and Hidayati

et al. showed almost the same prevalence of dysmenorrhea, namely 82.3%, with the majority of the intensity of dysmenorrhea being mild and 82.1% with the majority being the moderate intensity of dysmenorrhea. In Bahri et al.'s study, the intensity of dysmenorrhea was assessed based on interviews using a questionnaire measuring instrument conducted on 96 people in West Sumatra.¹⁷ Hidayati et al.'s research was conducted in Surakarta with a total of 67 female respondents. This study assessed the intensity of dysmenorrhea using a universal pain assessment tool.¹⁶ In a study conducted on adolescent girls in Japan, the prevalence of dysmenorrhea was 85%.¹⁸ In this study, the pain sensitivity questionnaire was used, which assessed several factors more than the visual analogue scale used in this study.

This study concluded that there was a relationship between calcium intake and the intensity of primary dysmenorrhea ($p = 0.000$). These results are in accordance with research conducted by Razzak et al. on 127 Jordan University of Science and Technology students aged 19 - 24 years that there is a relationship between intake of dairy products and a decrease in dysmenorrhea complaints ($p=0.000$).⁵ Dairy products themselves are a source of food that is high in calcium content.⁷ Research conducted by Tih F et al. at the University in Bandung City on 60 female students aged 19-23 years who experienced symptoms of premenstrual syndrome and dysmenorrhea, it was found that consumption of calcium or magnesium supplements reduced complaints of dysmenorrhea and symptoms of premenstrual syndrome ($p=0.000$).⁹ Calcium affects the permeability of nerve membrane. As a stabilizer, calcium can regulate muscle cells in response to nerve stimuli through various pathways. Decreased levels of calcium in the blood cause muscle spasms and contractions.¹⁹ Muscle contractions that last a long time cause ischemia and hypoxia of the uterine muscles, which ultimately lead to dysmenorrhea.²⁰ In a study conducted by Hidayati KR et al. The results showed that most respondents with low calcium intake felt moderate pain. Respondents with normal calcium intake showed less dysmenorrhea than those with low calcium intake. The study stated that the higher the calcium intake, the less the intensity of dysmenorrhea ($r=-0.415$, $p=0.000$).¹⁶

In this study, calcium intake was measured using a semi-quantitative food frequency questionnaire (SQ-FFQ), which assesses food and beverage intake in the last month so that the accuracy highly depends on the respondent's memory. Further research suggests measuring levels of calcium in the blood so that it can accurately describe the effect of calcium on the intensity of dysmenorrhea. This study did not analyse other factors that influence dysmenorrhea, such as stress, smoking, family history of dysmenorrhea, and intake of vitamin D and magnesium.

CONCLUSION

The prevalence of adolescents with low calcium intake is 51.6%. About 75.8% of respondents experienced primary dysmenorrhea, and 45.2% of them experienced moderate to severe dysmenorrhea. There is a relationship between calcium intake and the intensity of dysmenorrhea. Further research is needed with different methods to explain the causal relationship between calcium intake and the intensity of dysmenorrhea and other variables that affect the intensity of dysmenorrhea.

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AUTHORS CONTRIBUTION

Authors contributed to the manuscript writing, data collection and analysis. AD contributed to the improvement of the script. All authors have read the final manuscript and gave their consent.

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CONFLICT OF INTEREST

Competing interests: No relevant disclosures.

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