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The correlation between plasma malondialdehyde levels and pain in adolescent females diagnosed with primary dysmenorrhea

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ABSTRACT

Background: Endometrial inflammation factors play a crucial role in the common pathophysiology of primary dysmenorrhea. Malondialdehyde (MDA), a byproduct of inflammatory processes, might be correlated with primary dysmenorrhea in adolescents.

Objective: To assess plasma MDA levels in patients with primary dysmenorrhea.

Methods: This cross-sectional study involved the collection of blood samples from 23 teenage females with primary dysmenorrhea and 23 age-matched individuals without this condition. Plasma MDA levels were determined using spectrophotometry. The independent t-test was employed to ascertain the disparity in plasma MDA levels between the two groups, while the Pearson correlation test was utilized to analyze the relationship between pain severity and oxidative stress levels.

Results: Plasma MDA levels significantly higher in women with primary dysmenorrhea than in the control group (0.631 ± 0.105 and 0.395 ± 0.076, respectively). A significant difference in oxidative stress levels between the case and control groups ($p<0.001$). Furthermore, a robust positive correlation was observed between plasma MDA levels and pain severity in adolescent girls with dysmenorrhea ($r^2 = 0.564$, $p<0.001$).

Conclusion: The plasma MDA is increased in adolescent females with primary dysmenorrhea.

Keywords: Malondialdehyde, oxidative stress, primary dysmenorrhea

Introduction

Dysmenorrhea is a common symptom among women of reproductive-aged, can be classified into two types: primary and secondary [1]. Primary dysmenorrhea characterized by menstrual cramps, a painful absence of obvious pathology, and a common gynecologic disorder in women aged 18-28 [2]. Most adolescents are uncomfortable during menstruation [3]. The prevalence of dysmenorrhea stands at approximately 41%, and 91.5% of school-aged, young women, and university-aged individuals being affected by dysmenorrhea [4]. Furthermore, severe dysmenorrhea in adolescents has been shown to have a detrimental impact on their quality of life and academic performance [5–7].

Primary dysmenorrhea etiology remains unclear; with vatious theories suggesting the involvement of endometrial inflammation factors [8, 9]. Additionally, heightened intrauterine secretion of prostaglandin F2α (PG-F2α) and prostaglandin E2 (PGE2) is responsible for pelvic pain in primary dysmenorrhea [9–12]. Furthermore, the differences in oxytocin, vasopressin, FSH, and 17β-E2 concentrations found in women with dysmenorrhea plasma suggest an involvement of these hormones in mechanisms of primary dysmenorrhea [13].

Oxidative stress has been implicated in over a hundred diseases, including dysmenorrhea [9, 14]. A lipid peroxidation process markers oxidative stress in cells and tissues. It is characterized by a

balance between the production of free radicals and the antioxidant defense system. Furthermore, lipid peroxides break down into malondialdehyde (MDA), which is also a byproduct of prostaglandins [15]. Numerous studies have reported that dysmenorrhea increased lipid peroxide as an index of oxidative stress [16–18]. This heightened lipid peroxidation process will activate inflammatory mediators in the endometrium, leading menstrual pain.

A study involving women aged 20 to 39 demonstrated an increase in oxidative stress among individuals with dysmenorrhea [9]. However, it remains unknown what the oxidative stress status is in adolescents aged (10-19 years old). Further evidence in different age groups is needed. Furthermore, it remains uncertain whether oxidative stress levels among adolescents with primary dysmenorrhea are different compared to healthy controls. Therefore, this study aims to analyze plasma MDA levels in Primary dysmenorrhea.

Methods

Design of study

The study was conducted from August to December 2021. It was a cross-sectional study. The location of this study was Pondok Pesantren Al-Fatah Palembang and Bio Sains Riset Laboratory, Palembang.

Ethical clearance

Participants agreed as subjects and signed the informed consent prior to the study. The Health Research Ethics Commission of Politeknik Kesehatan Kementerian Kesehatan Palembang granted ethical clearance approval, numbered 1152/KEPK/Adm2/VIII/2021.

Subject and samples of study

Forty-six adolescents aged 10-19 years were obtained in this study as the subjects. The subjects were divided into two groups, namely 23 adolescents (females) in the dysmenorrhea group and adolescents without dysmenorrhea (control group). In the dysmenorrhea group, we set the following criteria: pain occurs 6-12 hours after menstruation; Pain in the lower abdomen or pelvis and medial or interior thigh pain associated with early menstruation; pain lasts at least 8 hours during menstruation; Pain can be followed by other symptoms such as headache, diarrhea, nausea, and vomiting [9].

Plasma MDA measurement

Each participant drew 5 ml of whole blood from a peripheral vein using an EDTA vacuum tube. Blood plasma was separated from whole blood by centrifugation at 3500 rpm for five minutes. The separated plasma was then transferred to a new tube and stored until use at -80^{0}C. The plasma MDA level was determined using the protocol from previous research [19], specifically utilizing the TBA method. MDA levels were measured at the BioScience Research Laboratory, Palembang. Plasma MDA are expressed in accordance with international standards as nanomoles per milliliter (nmol/mL).

Pain measurement

The pain level is measured at 8-72 hours of menstruation. Additionaly, we confirmed the menstrual pain experienced three months prior by each participant. Faces Pain Scale-Revised (FPS-R) questionnaire was used to measure the pain level [20]. The interviewed and technical measured pain levels followed the previous study [21].

Data analysis

For statistical measurements, version 21 of SPSS software was used. Shapiro-Wilk was used to determine the normality test. Spearmen's correlation test was used to analyze the relationship between plasma MDA and pain level in primary dysmenorrhea. A linear regression analysis was performed to determine the effect of plasma MDA on pain levels in patients with primary dysmenorrhea. In addition, an independent T-test was used to determine the difference in oxidative stress between those with and without dysmenorrhea. Statistical significance if the p-value is less than 0.05.

Table 1. Subject characteristics

Variables	Primary dysmenorrhea (mean ± SD)	Without primary dysmenorrhea (mean ± SD)
Aged (year)	16.26 ± 1.356	16.13 ± 1.486
Height (cm)	154.26 ± 6.232	154.74 ± 5.643
Weight (kg)	50.39 ± 8.033	49.43 ± 8.564

Results

The characteristic of the participants is described in Table 1. The average age of participants was approximately 16 years old in both groups. The mean height and weight were found between both groups about 154 cm and 50 kg.

Figure 1 shows that the pain level of primary dysmenorrhea was higher than no primary dysmenorrhea (mean ± SD = 6.43 ± 1.037 and 2.17 ± 0.778, respectively). Plasma MDA level of primary dysmenorrhea was increased than control (mean ± SD = 0.631 ± 0.105 and 0.395 ± 0.076, respectively). In addition, plasma MDA and pain levels in the primary dysmenorrhea were significantly different compared with the control (p-value < 0.001) (Figure 2).

According to the Spearmen test and the linear regression (Figure 3), there was a significant correlation between plasma MDA and pain levels in primary dysmenorrhea (p-value <0.001). Furthermore, plasma MDA affected the paint level in primary dysmenorrhea by 56.4% (value of R square = 0.564).

Discussion

This study found that plasma MDA in adolescents (female) and pelvic pain levels in primary dysmenorrhea subjects were significantly higher than those without primary dysmenorrhea (Figure 1). Primary dysmenorrhea is characterized by abdominal or low back pain for at least two days during menstruation and no apparent organic disorder [22]. Increased ischemia of the uterine myometrium during contractions can lead to the accumulation of free radicals. It is involved in the pathogenesis of dysmenorrhea [23, 24]. Oxidative stress plays a vital role in uterine endothelial dysfunction and the severity of dysmenorrhea [25, 26].

We found that plasma MDA levels in primary dysmenorrhea in female adolescents increased in line with the current study of young Nigerian women [27]. Elevated malondialdehyde (MDA) is commonly used as a marker of lipid peroxidation when pathophysiological processes occur in humans [28]. In addition, previous studies have found that plasma levels of MDA, serum nitric oxide (NO), and adrenomedullin (AM) are increased in primary dysmenorrhea [16, 29–31].

This study also identified a significant relationship between plasma MDA levels and pain levels on the incidence of primary dysmenorrhea in adolescents (females) (Figure 3). In this study, the elevated plasma MDA levels in young women with dysmenorrhea may be related to inflammation during menstruation. Another study stated that increased plasma MDA is accompanied by excess ROS production and antioxidant deficiency in several diseases associated with inflammatory factors [32–35]. In addition, inflammatory cells are one source of endogenous ROS produced by reducing molecular oxygen [36]. Furthermore, dysmenorrheal pain occurs due to increased macrophage activity which is characterized by increased inflammatory reactions in the endometrium and results in nociceptive nerve fiber transduction [37].

Revealing the relationship between oxidative stress and primary dysmenorrhea can be considered in prevention, diagnosis, and therapy. Plasma MDA serves as an oxidative stress marker, but it is insufficient to determine the general pathogenesis of primary dysmenorrhea. However, the advantages of measuring plasma MDA levels are accessibility, effectiveness, and cost-effectiveness when compared to other oxidative stress markers.

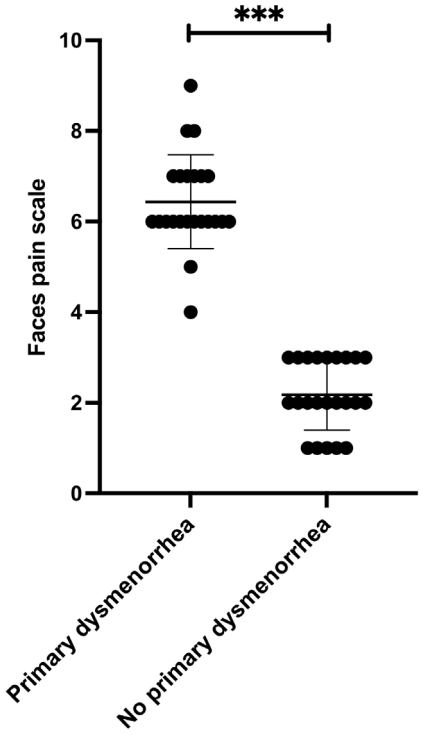

Figure 1. The difference of pain levels between primary dysmenorrhea and no primary dysmenorrhea. Pain level was analyzed using Mann-Whitney. ***p-value <0.01

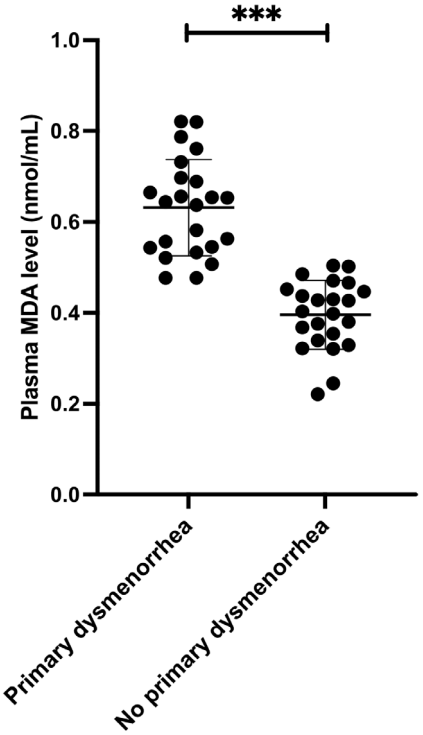

Figure 2. The difference of plasma MDA between primary dysmenorrhea and no primary dysmenorrhea. Plasma MDA level was analyzed using the independent T-test. ***p-value <0.01

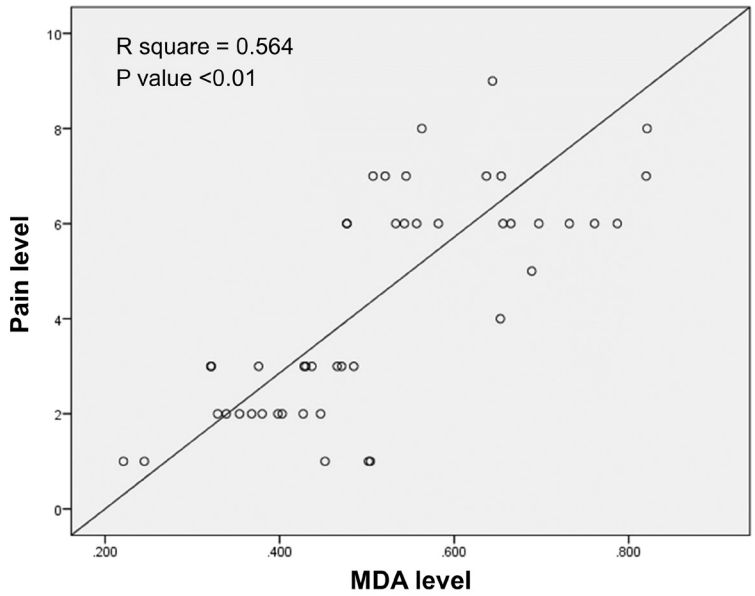

Figure 3. Correlation between plasma MDA and pain levels in primary dysmenorrhea

Conclusion

Plasma MDA is altered and increased in adolescent females with primary dysmenorrhea.

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Author contributions

All authors contributed to conceptualization, methodology, validation, investigation, resources, data analysis, writing, visualization, and supervision in this study.

Declaration of interest

There was no conflict of interest in this study.

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