A New Insight on Atopic Skin Diathesis: Is It Correlated with the Severity of Melasma

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Abstract: Melasma is a macular lesion of light brown to dark on the sun-exposed area, especially on the face. Atopic Skin Diathesis (ASD) is a clinical term to describe skin atopics with previous, present or future atopic dermatitis (AD). Dennie-Morgan infraorbital folds are secondary creases in the skin below the lower eyelids with a sensitivity of 78% and a specificity of 76% to diagnose AD. Melasma skin is characterized by impaired stratum corneum integrity and a delayed barrier recovery rate. Barrier dysfunction will stimulate keratinocyte to secrete keratinocyte-derived factor, which plays role in skin pigmentation process in melasma. To analyze correlation between ASD and Melasma Area Severity Index (MASI) score in melasma patient. This study is an observational analytic study with cross sectional design. Measurement of ASD and MASI score were done in 60 subjects with melasma who went to dermatology outpatient clinic Dr. Sardjito General Hospital from July 2017 to Januari 2018. The correlation between ASD and MASI score was analyzed using Pearson correlation. The result of this study showed no significant correlation between ASD and MASI scores (r: 0.02, *p*: 0,85). Crude Relative Risk (RR) for Dennie-Morgan infraorbital folds and MASI score was 4 (1.01-15.87). There was no correlation between ASD and MASI scores. Patient with Dennie-Morgan infraorbital folds has 4 times higher risk for developing severe melasma.

1 INTRODUCTION

Melasma is a hyperpigmented disorder of macular or patches lesions with light brown to dark, irregular edges and firm borders. Lesions are usually symmetrical on the sun exposed area especially on the face, primarily affects female patients and tends to be chronic and relapsing. In Indonesia the prevalence of melasma is estimated about 0.2 - 4% of all cases of skin diseases (Kim *et al.*, 2007; Hernández-Barrera *et al*., 2008). Melasma can cause pigmentation which is detrimental to patients' psychological well-being and bring adverse consequences in their social life, recreational activities, and emotional well-being for a long period of time (Kang *et al.*, 2002). Due to the chronicity of the disease, treatment of melasma should take a minimum of 8 weeks with a considerably high cost. Despite the high cost of treatment, this disease is chronic and recurrent without any guarantee of full remission. Most clinician usually use (Melasma Area Severity Index) MASI score to evaluate treatment in melasma. The MASI score showed good reliability within and between raters and was found to be valid when compared with the melasma severity scale, mexameter scores, and area measurements (Berardesca & Maibach,1996).

The cause of melasma is not yet known, but several factors are thought to play a role in the etiopathogenesis of melasma. The interaction of keratinocytes may also be involved in melasma: the activation of inducible nitric oxide synthase (iNOS) and Keratinocyte Derived Factor (KDF) within keratinocytes particularly after ultraviolet (UV) radiation, has a role in melanogenesis process (Reed *et al*., 1995). Impaired skin barrier is one of the underlying mechanism in melasma pathogenesis. This condition is also commonly found in atopic dermatitis patients. Several scoring systems have been proposed to assess the degree of skin barrier impairment. Among the most commonly used

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scoring system is Atopic Skin Diathesis (ASD) score which are calculated based on atopic symptoms and signs for practical use and for clinical or epidemiological studies (Kompaore *et al*., 1993). A total of 13 components are assessed in the calculation of ASD score, many of which are associated with imparied skin barriers, including keratosis pilaris, xerotic skin, pityriasis alba, and Dennie-Morgan infraorbital folds. However, the scoring system is usually used to diagnose atopic dermatitis.

Given that skin barrier impairment is found in both melasma and atopic dermatitis we thought that ASD score might also be of use in assessing melasma patients. In this study, we would like to investigate the correlation betwen the ASD score and severity of melasma.

2 METHOD

This is an analytic cross-sectional study that included 60 melasma patients who went to dermatology outpatient clinic at Dr. Sardjito General Hospital from July 2017 to Januari 2018. Measurement of both ASD and MASI score were done for those patients. Descriptive characteristics for the subjects were presented. The correlation between ASD and MASI score was analyzed using Pearson correlation. Further, MASI score was divided into two categories, <18 (low) and ≥18 (high). Crude relative risk (RR) was calculated to assess the risk of higher MASI score associated with each component of ASD score.

3 RESULT

The descriptive summaries of enrolled subjects were presented in Table 1. The age of the subjects ranged from 32 to 61 years old with an average of 46.65 years old. Centrofacial was the most common type of melasma (83.3%) followed by malar type (16.67%). Skin type IV accounted for 70% of the subjects.

Table 1. Descriptive summaries of the subjects

	Mean ± SD	**Number of subjects (%)**
Age, years	46.65 ± 5.96	-
Minimum age	32	-
Maximum age	61	-
Length of disease, years	7.8	-
Minimum duration	0.5	-
Maximum duration	20	-
Skin Type		
III	-	10(16.67)
IV	-	42(70)
V	-	8(13.33)
Melasma Type		
Malar	-	10(16.67)
Mandibular	-	0
Centrofacial	-	50(83.3)
MASI score		
<18	-	53(88.83)
≥18	-	7 (11.67)
ASD score		
<10	-	55(91.67)
≥10	-	5(8.33)

ASD: atopic skin diathesis
MASI: melasma area severity index

A relatively large proportion of subjects were found to have lower scores of MASI (88.83%) and ASD 91.67%,). While the majority of subjects were in the group of having lower MASI and ASD scores, a Pearson correlation test that had been carried out did not result in a significant correlation between ASD and MASI scores (r:-0.02, p:0.85) (Figure 1).

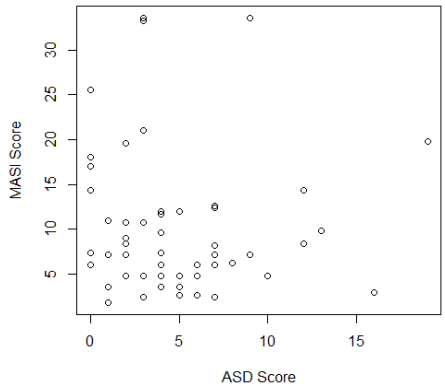

Figure 1. The scatterplot of ASD score vs MASI score.

Additional analysis was also carried out to analyze the relationship between ASD score and MASI score after categorizing them into two groups (lower or higher score groups) as in Table 1. However, we did not find any significant association between those two categorical variables (results not presented here).

This figure did not show any pattern of correlation between both scores, as later supported by a Pearson correlation test (r:-0.02, p: 0.85). Further, we calculated the crude relative risks (RR) for having more severe melasma, indicated by a higher category of MASI score (≥18), for each component that contributed to the calculation of ASD score. Of all components, the presence of intraorbital folds was the only factor that appeared to be significantly associated with higher risk of severe melasma (RR: 4.00(1.01-15.87)).

Except for keratosis pilaris, other components of ASD score related with skin barrier impairments (the presence of xerotic skin and pityriasis alba) showed a trend towards a higher risk of severe melasma, even though the relationship did not appear to be statistically significant (Table 2). In particular, we could not calculate the RR for keratosis pilaris since none of our subjects in this study were found with that condition.

Table 2. Relative risk for having higher MASI score (≥18) for each component of ASD score

ASD Score Components	Relative Risk (95% CI)*
Total number of subjects = 60	
Cradle cap	0.94 (0.13-6.94)
Intraorbital fold	4.00 (1.01-15.87)
Perleche	0.39 (0.02-6.29)
Pityriasis alba[#]	1.83 (0.27-12.36)
Ear rhagade	2.00 (0.17-24.17)
Palmar hyperlinearity	0.94 (0.13-6.94)
White Demographism	3.03 (0.72-12.76)
Xerosis[#]	2.00 (0.45-8.89)
Itchy while sweating	0.21 (0.01-3.45)
Fotofobia	0.55 (0.07-4.17)
Wool Intolerance	3.03 (0.72-12.76)
Food Intolerance	0.31 (0.02-5.02)
Allergic Rhinitis	0.29 (0.04-2.24)
Asthma	1.50 (0.22-10.46)
Sensitivity to Metal	0.33 (0.04-2.58)
Atopic History in Family	3.11 (0.77-12.51)

ASD: atopic skin diathesis
*Values are crude (unadjusted) relative risk (95% confidence interval)
[#]Components that are related with skin barrier impairment

4 DISCUSSION

Our study contributes to building evidence on the use of ASD score in evaluating melasma. To our knowledge, this is the first study that assess the relationship between ASD score and severity of melasma. A larger sample size would be required for a more comprehensive analysis on the use of ASD score in evaluating melasma. In our study, more than 80% of subjects were found to have both lower MASI and ASD score. This is one of the major limitations of our current study. Since the patients recruited for this study were regular patients at Dr. Sardjito General Hospital who had received treatment based on the standard protocol, i.e, they were not newly diagnosed patients with melasma.

The mean duration of disease of the subjects were 7.8 years, so it was very likely that the disease has evolved throughout those years.

The characteristic of the subjects in this study showed that centrofacial type was the most common type of melasma (83.3%) followed by malar type (16.67.%), in accordance with previous research which reported that most types of melasma were centrofacial type followed by malar and mandibular type (Kim *et al.*, 2007; Hernández-Barrera *et al*., 2008). Centrofacial type is most often found in women, whereas malar type is more often found in men. This is thought to be related to the predominant occupational activity outside the home in male patients.

The result of this study is similar to the previous studies with majority of the subjects aged between 40 to 50. However, as we only included patients who went to Dr. Sardjito Hospital during our study period, our sample could not be considered as representative of the real melasma patients in the population. Our study, in which the majority of subjects were found to have skin type IV, is in accordance with previous studies in Brazil. Our subjects (70%) have skin type IV and little portion of skin type III (16.67%) and type V (13.3%) (Reed *et al*., 1997; Kang *et al*., 2010).

Our results suggest Dennie-Morgan infraorbital folds as the only ASD score component being significantly associated with higher risk of severe melasma. However, interpretation of our results should be done very cautiously. The relative risks calculated in this study were crude relative risks, i.e., the calculation was carried out without taking into account (adjusting to) any other parameters that might simultaneously affect the risk of having more severe melasma. Further analysis with adjustment to other potential confounders is, therefore, necessary.

Dennie-Morgan infraorbital folds are secondary creases in the skin below the lower eyelids. They are a minor criterion of AD and are present in up to 84% of patients with AD, with a sensitivity of 78% and a specificity of 76%. They are also described in patients with allergic rhinitis and/or asthma without AD (Kang *et al*., 2006; Merle *et al*., 2010). The pathophysiology is not clearly established. They may be related to skin edema and the continuous spasm of the Muller eyelid muscle resulting from hypoxia linked to poor blood circulation. Finally, our research supports the idea that impaired skin barrier might be a common underlying mechanism that mediates the link between atopic conditions with melasma. Further investigation is necessary to provide the evidence on this relationship.

5 CONCLUSION

We did not find any correlation between ASD and MASI scores. More in-depth research on ASD score can be used to investigate the alleged causal relationship in melasma.Examination of ASD score is not a routine examination of melasma patients and other oxidative stress disorders, so another indicator is required in measuring skin barrier function.

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