ORIGINAL ARTICLE

Energy and Dietary Intakes in Adult Atopic Dermatitis

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ABSTRACT

Introduction: Studies on nutrition among adult AD, a chronic inflammatory skin condition, are lacking. The objective of this cross-sectional study was to investigate the energy, micro and macro nutrient intakes. **Methods:** Sixty two adult participants defined by the Hanifin-Rajka criteria were included. AD severity was determined using SCORAD index and objective SCORAD. Demographic data and a three-day 24-hour dietary recall were collected and analyzed. Basal metabolic rate (BMR) was estimated using Schofield's equation. The Energy Intake (EI): BMR ratio was used to identify under reporters (EI:BMR<1.2). To understand food preferences, main food groups consumed, meat (chicken, beef, and pork), seafood (fish, crustaceans, and mollusk), vegetables, fruits, including eggs and milk were examined. To ascertain food avoidance, open ended questions were asked. **Results:** Significant differences between the severity of AD groups and energy intake, vitamin A, beta carotene, magnesium, and energy intake-basal metabolic rate ratio (EI: BMR) were seen for SCORAD index. Energy intake was significantly lower among severe AD. Vitamin A and magnesium intake was lower among severe AD. Saturated fat intake was higher among mild AD. EI: BMR was inversely correlated with objective SCORAD. Seventy seven percent of participants were under reporters. Almost 10 percent reported avoiding some form of seafood; predominantly form the crustacean or mollusk group. **Conclusion:** Subjective symptoms, a component of SCORAD index but not objective SCORAD, may have contributed to significant differences seen. Lower energy intake in severe AD was due to reduced dietary intake during flares rather than underreporting.

Keywords: Atopic dermatitis, Eating, Beta carotene, Fatty acids, Magnesium

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INTRODUCTION

Atopic dermatitis (AD) is a chronic remitting inflammatory disorder affecting the skin. It is closely related to the other atopic conditions namely, allergic rhinitis, bronchial asthma, and allergic conjunctivitis. It is a common disease among the pediatric age group but there is a small group of patients where the disease progress into adulthood, has its onset during adulthood or even after the age of sixty. The abnormal immune response in AD is mainly propagated by T-helper (Th)2-phenotype (1). There are many studies on various dietary aspects of atopic dermatitis, which are focused on specific foods or nutrients and concerning food allergies. An excessive intake of n-6 polyunsaturated fatty acid (PUFA) promotes the Th2-skewed immune responses and exacerbates the symptoms of AD, while n-3 polyunsaturated fatty acid (PUFA) has the opposite effect(2).

To our knowledge, there have only been a handful of studies in dietary intake in adult AD in Asia. A case-control study by Ito et al. (3), found that patients with atopic dermatitis had higher intakes of carbohydrates and potatoes and lower intakes of alcohol, niacin(vitamin B3), meat, and oils/fats compared with those of the healthy controls. Pyridoxine (Vitamin B6) intake was a predictor of AD severity(3). Vegetable fat, n-6 polyunsaturated fatty acid, and confections consumption were lower among the severe AD patients than those in the mild group. A study in Korea found a higher prevalence of AD in those who consumed processed food, instant noodles in particular, and meats (4).Similar studies in Korea also found that intake of fermented foods had beneficial effects on AD(5,6).Dietary habits are unique to a population. In Malaysia, cultural diversity translates to a diverse practice of nutritional habits. There has been one study on food restrictions and dietary intake among toddlers(7) with AD in Malaysia but none among the adult population. Basic dietary studies like this can give insight into the role that nutrition plays in the pathophysiology of this condition. The diagnosis of atopic dermatitis using the Hanifin and Rajka criteria requires that patients have at least three major and

three minor criteria (8). The objective was to assess the energy and dietary intake of adult Malaysian AD patients attending the dermatology clinic in Universiti Kebangsaan Medical Centre (UKMMC). We also compared differences in stratifying the participants' AD severity according to SCORing Atopic Dermatitis index (SCORAD Index) and objective SCORAD.

MATERIALS AND METHODS

Study Design

This was a cross-sectional prevalence study. Participants, who fulfilled the inclusion criteria, patients aged 18 and above diagnosed with AD according to the Hanifin-Rajka criteria (8), were included. The sample size was calculated using the following formula, using inputs from a study by Michiko et.al(3) and estimated prevalence of adult AD in Malaysia(9). The sample size formula: n= Z2 P(1-P)/d2 where n = sample size, Z = Z statistic for a level of confidence 95% in this study, P = expected prevalence (4%, P = 0.04), and d = precision (in proportion of one; if 5%, d = 0.05). Minimal sample size required is 59. Patients with AD and other Inflammatory or Autoimmune co-morbidities were excluded. Data were collected from eligible subjects who had consented to the study. Patients' dietary intake was analyzed using Nutritionist ProTM (Axxya Systems) Diet Analysis Software (2007) for macronutrients and micronutrients. Statistical Package for Social Sciences (SPSS) ver 26.0 was used for data analysis. ANOVA (analysis of variance) was used to determine if there were significant differences in means between mild, moderate and severe AD. A Tukey post-hoc analysis was done to analyze differences in means between mild-moderate, moderate-severe, and mild-severe AD. Pearson's correlation test was used to determine correlation between nutrients, and the 2 SCORADs. The study was approved by the medical research and ethics committee of Universiti Kebangsaan Malaysia (National University of Malaysia) with an allotted project code FF-2020-473.

Demographic and SCORAD questionnaire

Demographic data on the participants' age, gender, allergies, food avoidance (if any), height, and weight were collected. SCORAD, stratifies atopic dermatitis (AD) into mild, moderate, and severe. It was carried out to document the severity of AD during the interview. Two types of SCORAD, SCORAD Index and Objective SCORAD were used (10). Objective SCORAD excluded the subjective symptoms of the participants. While both are valid measures of AD severity, we included these two measures to study if the participant's subjective symptoms had a bearing on dietary intakes. The SCORAD index consists of the interpretation of the extent of the disorder (A: according to the rule of nines – 20% of the score), the intensity composed of 6 items (B: erythema, edema/papules, the effect of scratching, oozing/crust formation, lichenification, and dryness – 60% of the score; each item has four grades: 0, 1, 2, 3) and subjective symptoms (C: itch, sleeplessness –20% of the score).

Subjective symptoms are not included in Objective SCORAD(10).Severity in the SCORAD index is classified as mild (<25), moderate (25-50), and severe (>50). The maximum score is 103. For Objective SCORAD, with the highest score being 83, severity classified as mild (<15), moderate (15-40), and severe (>40)(10).

24-hour dietary recall

A 24-hour dietary recall is a structured interview conducted by the investigator on the research participant to obtain detailed information on foods and beverages consumed by the participant over 24 hours. It includes all the types of foods, drinks, and dietary/nutritional supplements. The interview is either done face to face or via telephone. It is used widely in population surveys and research (11–13).

Based on memory, participants provided dietary information about their consumption in the past 24-hours. They described the type of food or beverage consumed and portion size and cooking methods (if applicable). Their first food intake from the time they woke up till their last intake before bed was recorded. The interview was based on the multiple pass method. Participants are first asked about all the food they consumed within the last 24-hours (Pass 1), followed by a thorough probing whereby they detailed information for each food/ beverage, for the type, amount, any addition to the food/ toppings, preparation methods including the type of oil/ fat used is obtained (Pass 2). To assist the participants with their memory, they were asked to recall when the food/ beverage was consumed, as well as the place. If the food was packaged, the brand name, as well as the amount consumed, was obtained. A final pass of the interview included reviewing the foods and amount consumed, providing the interviewee a chance to correct any inaccurate information (13,14). Participants received a food guide consisting of Malaysian household measures (cups, bowls, tablespoon, teaspoons, glasses) to help recall the portion size (15,16). Previous studies have used this method. Three dietary recalls were collected, two weekdays and one weekend. The first recall was conducted during the first visit while the remaining two, were conducted via telephone. All recalls were completed within the week, at the participants' convenience. If they were unavailable during the scheduled phone call, an alternative appointment was set within the same week. A picture guide to help indicate food portions consumed was given to participants. Patients' dietary intake was analyzed using Nutritionist ProTM (Axxya Systems, San Bruno, CA) Diet Analysis Software (2007) for macronutrients and micronutrients. Each food or beverage item and portion size from the dietary recall was entered into Nutritionist Pro by matching with appropriate items listed within the software. Composite dishes and mixed dishes were analyzed by adding the

recipe into the software by entering it as single items. The Nutritionist pro software contains Malaysian Food composition databases as well as other international databases such as USDA Food Database, Canadian Food Database, and Mexican Food Database. When they were no match for a food item on the Malaysian database were found, borrowed data from international databases were used.

The basal metabolic rate (BMR) was estimated using Schofield's equation. The Energy Intake (EI): BMR ratio identified under reporters. Classification of the EI: BMR ratio into under reporters (EI: BMR<1.2), plausible (EI: BMR 1.2-2.4), and over reporters (EI: BMR>2.4) were used(17,18). This method of identifying EI misreporting has been used in other dietary intake studies involving the Malaysian population (19–21).

A detailed understanding of food preferences or avoidances in AD participants was not part of this study's design. Nevertheless, we looked at the major food groups consumed, as reported in the three-day 24-hour dietary recall, by mild and severe AD, classified according to SCORAD Index. The main food groups we examined were meat (chicken, beef, and pork), seafood (fish, crustaceans, and mollusk), vegetables, and fruits. Eggs and milk were two food items frequently correlated to food allergy and increased risk of anaphylaxis in AD cases. Peanut allergic patients with and without AD had similar rates of anaphylaxis. Egg and milk allergic patients with AD exhibited increased anaphylaxis compared with those without AD (22). We also asked patients open-ended questions if they avoided certain foods and reasons for doing so. These questions provided information if the participants were allergic to particular foods or if it merely triggered AD flares.

RESULTS

There were 62 adult AD participants in this study. Tables I and II describe the participants' demographic data, estimated basal metabolic rate (BMR), Energy Intake (EI), EI: BMR ratio, and mean macro and micronutrient intake corresponding to AD severity using SCORAD index and objective SCORAD. There were a total of sixty two AD participants in this study. Eighteen (29%) were males and forty-four (71%) were females. The majority of the participants were Malays (56.5%) followed by Chinese (27.4%) and Indians (16.1%). The mean BMI of participants was 25.96 ± 6.26SD.Among the sixty two subjects, only three (4.8%) were underweight. Thirty (48.4%) had normal BMIs, sixteen (25.8%) were overweight, and thirteen (21.0%) were overweight. The mean age of participants was 34.6 ± 14.8SD.SCORAD index and Objective SCORAD were two measures of severity for AD employed. Their mean scores were 30.54 ± 15.7SD and 21.28 ± 17.4SD, respectively.

There was a significant difference between the severity (SCORAD Index) of AD groups for energy intake (p=0.035), vitamin A (p=0.008),beta carotene (p=0.020), magnesium (p=0.013), and EI: BMR ratio (p=0.014) Table I. However, significant differences were not present when the Objective SCORAD was used, except for magnesium (p= 0.021).

Table I: Demographics and mean intakes of macro and micro nutrients using SCORAD index

	Mild	Moderate	Severe	Total	p-Value
	SCORAD Index				
Gender					
Male	6	6	6	18 (29)	
Female	23	15	6	44 (71)	
Ethnicity					
Malay	17	13	5	35 (56.5)	
Chinese	7	5	5	17 (27.4)	
Indian	5	3	2	10 (16.1)	
				Total Mean	
Age	36.40	34.00	31.60	34.60	0.628
BMI	26.70	24.60	26.60	25.90	0.461
BMI Class.(WHO)					
Underweight (BMI<18.5)	2	1	0	3	
Normal (BMI:18.5-24.9)	12	12	6	30	
Overweight (BMI:25.0-29.9)	6	6	4	16	
Obese (BMI>30.0)	9	2	2	13	
BMR(kcal)	1439.10	1427.05	1568.00	1459.97	0.276
EI (kcal)	1297.54^{ab}	1443.54^{a}	1064.95^{b}	1301.98	0.035*
Pro(g)	63.29	65.85	65.99	64.68	0.907
Carb(g)	164.07	185.90	145.70	167.91	0.135
Fat(g)	42.86	48.83	40.43	44.41	0.413
SFA(g)v	10.5	12.95	10.06	11.24	0.29
MSFAT(g)	9.25	9.11	10.37	9.42	0.792
PUFAT(g)	7.29	5.98	7.75	6.94	0.486
TFA(g)	0.33	1.03	0.70	0.65	0.24
Na(mg)	1559.73	1740.58	1718.61	1651.74	0.697
K(mg)	1368.8	1680.38	1432.13	1486.59	0.18
VitA (IU)	5622.23^{ab}	7817.97^{a}	4119.49^{b}	6075.10	0.008**
Beta Carotene(µg)	2237.70^{ab}	3204.66^{a}	1427.29^{b}	2408.36	0.029*
Lycopene(µg)	1357.62	815.57	3949.65	1675.71	0.149
VitC(mg)	80.2	95.05	68.58	82.98	0.574
Vit D (IU)	31.77	37.94	23.20	32.52	0.535
VitE (IU)	4.91	5.00	4.36	4.83	0.85
Thiamin(mg)	1.05	1.09	0.99	1.05	0.849
Riboflavin(mg)	1.17	1.22	1.07	1.17	0.742
Niacin(mg)	15.74	15.40	16.69	15.81	0.855
PyridoxB6(mg)	1.03	1.17	1.21	1.11	0.493
Folate (µg)	298.24	293.08	234.70	284.19	0.474
VitB12(µg)	2.44	2.72	2.75	2.59	0.919
Calcium(mg)	437.11	458.80	360.33	429.60	0.494
Iron(mg)	13.99	15.89	13.11	14.46	0.451
Magnesium(mg)	155.29^{ab}	217.20^{a}	155.22^{b}	176.25	0.013*
Zinc(mg)	5.26	5.97	5.14	5.48	0.497
Copper(mg)	0.8	0.87	0.66	0.80	0.303
Dfiber Tot.(g)	6.78	8.97	6.34	7.44	0.188
Sugar(g)	28.25	34.28	27.07	30.07	0.617
Glucose(g)	2.5	3.1	3.08	2.84	0.88
EI:BMR Ratio	0.92^{ab}	1.02^{a}	0.71^{b}	0.91	0.014*

**. Differences in mean are significant at the 0.01 level (2-tailed).
*. Differences in mean are significant at the 0.05 level (2-tailed).
Compact Letter Display - Tukey post-hoc analysis on significant ANOVA attributes:
a,b,c - denotes highest to lowest value of means (a – highest; c- lowest) if they are all significantly different; Tukey post-hoc analysis <0.05
ab – the mean is not clinically different compared to the remaining 2 means.

There was a significant difference between the severity (SCORAD Index) of AD groups for energy intake (p=0.035), vitamin A (p=0.008), beta carotene (p=0.020), magnesium (p=0.013), and EI: BMR ratio (p=0.014) Table I. However, significant differences were not present when the Objective SCORAD was used, except for magnesium (p= 0.021).

Table II: Demographics and mean intakes of macro and micro nutrients using Objective SCORAD

	Mild	Moderate	Severe	Total	p-Value
	Objective SCORAD				
Gender					
Male	6	8	4	18 (29)	
Female	19	18	7	44 (71)	
Ethniity					
Malay	16	13	6	35 (56.5)	
Chinese	5	9	3	17 (27.4)	
Indian	4	4	2	10 (16.1)	
				Total Mean	
Age	35.80	35.15	30.82	34.65	0.639
BMI	26.83	25.25	25.68	25.96	0.665
BMI Class.(WHO)					
Underweight (BMI<18.5)	2	1	0	3	
Normal (BMI:18.5-24.9)	10	13	7	30	
Overweight (BMI:25.0-29.9)	6	8	2	16	
Obese (BMI>30.0)	7	4	2	13	
BMR(kcal)	1454.28	1452.08	1491.55	1459.97	0.276
EI (kcal)	1388.84[a]	1324.99[ab]	1050.17[b]	1301.98	0.065
Pro(g)	66.13	66.78	56.44	64.68	0.423
Carb(g)	174.26	174.07	138.94	167.91	0.182
Fat(g)	47.35	45.55	35.06	44.41	0.198
SFA(g)v	11.73[a]	12.05[ab]	8.23[b]	11.24	0.195
MSFAT(g)	9.88	9.31	8.63	9.42	0.81
PUFAT(g)	7.80	6.12	6.92	6.94	0.431
TFA(g)	0.64	0.81	0.26	0.65	0.586
Na(mg)	1658.59	1669.72	1593.68	1651.74	0.965
K(mg)	1401.22	1634.75	1330.44	1486.59	0.241
VitA (IU)	5845.74	6722.24	5066.73	6075.10	0.398
Beta Carotene(µg)	2381.11	2713.21	1749.74	2408.36	0.387
Lycopene(µg)	931.86	1342.53	4153.78	1675.71	0.136
VitC(mg)	70.62	104.02	61.35	82.98	0.133
Vit D (IU)	34.48	35.86	17.58	32.51	0.367
VitE (IU)	4.95	4.80	4.64	4.83	0.964
Thiamin(mg)	1.08	1.11	0.85	1.05	0.348
Riboflavin(mg)	1.16	1.27	0.95	1.17	0.277
Niacin(mg)	15.78	16.28	14.76	15.81	0.807
PyridoxB6(mg)	1.02	1.21	1.08	1.11	0.431
Folate (µg)	320.18[a]	276.81[ab]	219.86[b]	284.19	0.195
VitB12(µg)	2.46	2.82	2.37	2.59	0.858
Calcium(mg)	471.64	429.17	335.05	429.60	0.268
Iron(mg)	14.66	15.02	12.69	14.46	0.614
Magnesium(mg)	158.43[ab]	208.20[a]	141.21[b]	176.25	0.021*
Zinc(mg)	5.38	6.04	4.37	5.48	0.137
Copper(mg)	0.84	0.82	0.63	0.80	0.28
Dfiber Tot.(g)	6.98	8.82	5.20	7.44	0.087
Sugar(g)	30.06	31.86	25.85	30.07	0.792
Glucose(g)	1.90	3.72	2.90	2.84	0.359
EI:BMR Ratio	0.98	0.92	0.74	0.91	0.076

*. Differences in mean are significant at the 0.05 level (2-tailed).

Compact Letter Display - Tukey post-hoc analysis on significant ANOVA attributes:

a,b,c - denotes highest to lowest value of means (a – highest; c- lowest) if they are all significantly different; Tukey post-hoc analysis <0.05

ab – the mean is not clinically different compared to the remaining 2 means.

Compact letter display (CLD) in Table I and II shows the means between mild-moderate, moderate-severe, and mild-severe groups classified according to SCORAD Index and Objective SCORAD. There were significant differences in vitamin A (p=0.029) and magnesium (p=0.005) between the mild and moderate groups classified using the SCORAD Index. There were significant differences between the moderate-severe AD group (Table I) for EI (p=0.02), vitamin A (p=0.029), and EI: BMR ratio (p=0.006). For the mild and severe group, significant differences were only for EI: BMR ratio (p=0.033).

For objective SCORAD, significant differences between the means for the moderate-severe group were found for folate (p=0.031) and magnesium (p=0.033). For the mild- severe group, significant differences were seen in EI (p=0.011), Fat (p=0.039), saturated fatty acids (SFA) (p=0.04), folate (p=0.047) and EI:BMR ratio (p=0.028).

There was a strong positive correlation between SCORAD index and Objective SCORAD (r=0.985; n=62; p<0.001) (Table III). Objective SCORAD and SCORAD Index, was inversely correlated with EI:BMR ratio, but only significant for Objective SCORAD (r=-0.293; n=62; p=0.021). Table III also showed significant correlations between dietary intake of magnesium and EI (r=0.541; n=62; p<0.001), total fat (r=0.391; n=62; p=0.02), saturated fatty acids (SFA) (r=0.448; n=62; p<0.001), EI:BMR ratio (r=0.450; n=62; p<0.001), folate (r=0.383; n=62; p=0.002), and vitamin D (r=0.304; n=62; p=0.019).

There were 48 (77.4%) under reporters (EI:BMR ratio <1.2) and 14 (22.6%) plausible reporters (EI:BMR ratio 1.2-2.4). There was no over reporters (EI: BMR ratio >2.4) among the participants (Table IV).

Chicken was the most consumed meat among the mild (22/29, 75.9%) and severe AD (10/12, 83.3 %) participants. Only non-Muslims, who were predominantly Chinese consumed pork and 2/29 (6.9%) of them had mild AD whereas 2/12 (16.7%) had severe AD. Participants who consumed beef were predominantly Muslims. One out of twenty-nine (3.4%) of them had mild AD and 1/12 (8.3%) had severe AD. In mild AD participants, 27/29 (93%) consumed seafood. Anchovies was the most common seafood consumed by 12/29 (41.4%), followed by indian mackerel fish 8/29 (27.6%). However, only 6 /29 (20.7%) mild AD participants consumed prawns. In contrast, only 6/12 (50%) severe AD participants consumed only fish. None of the severe AD participants consumed prawns. The most commonly consumed fish was the indian mackerel 3/12 (25%), followed by chinese catfish 2/12 (16.7%) and spanish mackerel 1/12 (8.3%). The severe AD group did not consume anchovies.

The most common vegetables consumed by mild AD participants were carrots 6/29 (20.7%), followed by swamp cabbage 4/29 (13.8%), chinese mustard leaves 3/29 (10.3%), and spinach 4/29 (13.8%). 12/29 (41.4%) consumed other vegetables including fern (pucuk paku), okra, long beans, french beans, cabbage, and mixed vegetables. Among the severe AD participants, the most commonly consumed vegetable was chinese cabbage (pak choy) 4/12 (33.3%), followed by chinese mustard leaves 3/12 (25%), broccoli 2/12(16.7%), lettuce (romaine lettuce) 1/12(8.3 %); iceberg lettuce 1/12(8.3%), and loofah, spinach, and tomato 1/12 (8.3 %).

Fruit consumption was generally poor among mild 5/29 (17.2%) and severe AD 3/12(25%) participants. The types of fruit consumed varied among the 2 groups.

TABLE III: Pearson correlations among SCORAD, energy intake selected nutrients, and EI:BMR

Variable	1.SCORAD	2.Obj. SCORAD	3.EI (kcals)	4.Total Fat (gm)	5.SFAT (gm)	6.VitA(IU)	7.BetaCaro (µg)	8.VitD(IU)	9.Folate (µg)	10.Magnesium (mg)	11.Zinc (µg)	12.EI:BMR
1	1	.971**	-0.162	-0.057	-0.013	-0.022	-0.043	-0.035	-0.119	0.065	-0.016	-0.230
2	.971**	1	-0.225	-0.132	-0.087	0.014	-0.007	-0.093	-0.120	0.065	-0.043	-.293*
3	-0.162	-0.225	1	.820**	.619**	0.215	0.116	.294*	0.212	.541**	.674**	.856**
4	-0.057	-0.132	.820**	1	.817**	0.106	-0.018	.308*	0.004	.391**	.651**	.643**
5	-0.013	-0.087	.619**	.817**	1	0.116	-0.005	.512**	0.011	.448**	.654**	.473**
6	-0.022	0.014	0.215	0.106	0.116	1	.906**	0.096	.262*	.474**	.293*	0.114
7	-0.043	-0.007	0.116	-0.018	-0.005	.906**	1	-0.022	.381**	.447**	0.213	0.019
8	-0.035	-0.093	.294*	.308*	.512**	0.096	-0.022	1	.264*	.304*	.441**	.275*
9	-0.119	-0.120	0.212	0.004	0.011	.262*	.381**	.264*	1	.383**	.332**	0.227
10	0.065	0.065	.541**	.391**	.448**	.474**	.447**	.304*	.383**	1	.771**	.450**
11	-0.016	-0.043	.674**	.651**	.654**	.293*	0.213	.441**	.332**	.771**	1	.510**
12	-0.230	-.293*	.856**	.643**	.473**	0.114	0.019	.275*	0.227	.450**	.510**	1

**. Correlation is significant at the 0.01 level (2-tailed).
*. Correlation is significant at the 0.05 level (2-tailed).

Table IV: Energy Intake: BMR ratio (EBR) classification of under, plausible, and over reporters

EI:BMR ratio (EBR) Classification	SCORAD Index Classification			
	Mild	Moderate	Severe	Total (%)
EBR <1.2 (under reporters)	23	14	11	48 (77.4)
EBR 1.2-2.4 (Plausible)	6	7	1	14 (22.6)
EBR >2.4 (over reporters)	0	0	0	0 (0.0)

The mild AD group consumed apples, oranges, grapes, banana, and kiwi fruit, while the severe AD group consumed guava, watermelon, and mango.

Eggs were consumed by 18/29 (62.1%) mild AD cases, compared to 5/12 (41.7%) by severe AD cases. Milk was consumed by 10 out of 29 (34.5%) mild AD participants compared to 3/12 (25%) by severe AD participants.

Overall, 6/62 participants (9.7%), reported food avoidance. All of them claimed to have avoided certain seafood, predominantly from the crustacean (prawns, shrimp, and crab) and mollusk group (cuttlefish, and squid). Out of these six participants, three were from the moderate AD group, three others were from the severe AD group. One of the participants from the severe AD group did not consume poultry meat.

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DISCUSSION

Data on energy and nutrient intakes among Malaysian adults is available from the Malaysian Adult Nutrition Survey (MANS), last carried out in 2014(23). MANS 2014 excluded cases that misreported EI. The mean EI for Malaysian adults was 2060 kilocalories (kcal). The mean EI for AD subjects in this study was 1301.98 kcal, which was very much lower than the average EI of the general Malaysian adult population. The macronutrient intake among the general Malaysian adult population was 81.0, 273.0, and 70.0 grams for protein, carbohydrates, and fat. Macronutrient intake among AD subjects was lower at 64.68, 167.91, and 44.41 grams for protein, carbohydrates and fat. These are mere comparisons and not statistically significant deductions.

Underreporting of energy intake is a recognized issue that has persisted in MANS throughout the years (21). The prevalence of underreporting in our study was 77.4%. In our study, we have reasons to believe that underreporting may have been affected by participants' symptoms. It became apparent, during data on 24-hour dietary recall collection, that a few of the severe AD participants had very low caloric intake. The low caloric intake did not commensurate with their BMI. On further query, they had restricted dietary intake during flares. EI: BMR ratios were significantly, inversely correlated to Objective SCORAD.

This indicated that lower EI: BMR ratios correlated with higher Objective SCORAD or more severe AD. This finding adds credence to the fact that underreporting was more prevalent in severe AD participants due to reduced caloric intake and not merely the act of underreporting itself. It is for this reason, energy intake adjustments were not made to address underreporting in this study. We acknowledge that there are limitations in addressing underreporting in this study, because underreporting may be a part of caloric restriction seen in more severe AD participants. It is an issue that must be addressed in future studies. Restricted energy intake, with increased calcium, iron, vitamin A, Vitamin C, and Vitamin E have been shown to reduce inflammatory symptoms of patients with AD (24).

The significance of lower energy intakes in severe AD participants was lost when objective SCORAD was used to stratify AD severity, which supports that the lower energy intake in severe AD is not due to underreporting. Future studies must address mechanisms to differentiate underreporting from reduced intake due to disease severity. Animal studies on the effects of beta carotene in AD have shown promising results. Translational studies on human subjects should follow through. Differences in cultural and diet habits may have caused varying outcomes in dietary and serum carotenoids in

human studies.

Social and cultural factors influence the subjective component of the SCORAD Index (10). In Objective SCORAD, this subjective component is removed. Although there was a strong correlation between Objective SCORAD and SCORAD Index, the exclusion of participant's symptoms in Objective SCORAD had significant differences in means. These findings suggest that participants' symptoms had a bearing on EI, vitamin A, beta carotene, and EI: BMR ratio.

One of the earlier studies done on magnesium and AD found that whole skin and dermal magnesium levels were significantly higher in adults with AD compared to healthy controls (1.5 – 0.4 vs. 0.9 – 0.4, respectively; $p < 0.01$), while epidermal magnesium content was not significantly different from controls (25). The frequency of hypomagnesemia (serum magnesium) was highest in AD than in controls, and contact dermatitis (0% in controls, 10% in contact dermatitis, and 16.7% in AD) (26).In a case-control study among the pediatric population, patients with AD had significantly lower serum magnesium levels and erythrocyte zinc (EZ) levels.

The SCORAD index did not correlate with serum concentrations of magnesium, EZ, copper, iron, and hemoglobin levels (27). Another case-control study on dietary habits among Japanese adults with AD did not show significant differences in magnesium intake between cases and controls. Correlations between SCORAD and magnesium intake were absent (3).

In animal studies, AD-like features in hairless mice fed diets low in magnesium was noted (28–30). In the study by Makiura, in addition to magnesium, the diet was also deficient in zinc(30). Zinc intake was not significantly lower in more severe AD but correlated with magnesium. Similarly, magnesium intake was also significantly correlated to other nutrients. Elucidating the role of significant correlations was beyond the objectives of this study. It should be considered in planning further dietary studies involving AD. These significant correlations may indicate how these different nutrients could relate synergistically during absorption. We showed that magnesium intake was significantly higher in moderate AD than in mild AD when using SCORAD index, and significantly lower in severe AD than in moderate AD when using Objective SCORAD. Recommended Nutrient Intake (RNI) for magnesium among Malaysian adults ranged from 400-420mg for males to 310-420mg for females (31). The mean magnesium intake for AD in this study was 176.25mg.

Vitamin A and beta carotene intake were significantly different across the groups when participants were classified according to SCORAD Index but not so when classified according to Objective SCORAD. Vitamin A intake was significantly higher in moderate AD than mild AD ($p=0.029$). Vitamin A ($p=0.002$) and beta carotene ($p=0.004$) intake were significantly higher in moderate AD than in severe AD.

Beta carotene is a naturally occurring vitamin A precursor and is most abundant among the other carotene isomers. Alpha and beta carotene plasma levels were higher in human controls than in AD cases but the differences were not statistically significant (32). No significant differences were also found between serum beta carotene levels in the atopic compared to the non-atopic group (33). In animal studies, however, oral administration of beta carotene improved the appearance of oxalozone induced AD-like skin in mice(34). Similar effects were also seen in zinc and magnesium-deficient diet-induced AD in murine models(35,36). In our study, Vitamin A and beta carotene intake differed significantly between the mild-moderate and moderate-severe groups for SCORAD index classification but not for the mild-severe group. No significant differences were found when participants were classified according to Objective SCORAD. Ito et al.'s study found no significant differences in beta carotene intake between AD and controls (3).A study on a pediatric population in Germany, consisting of native Germans, Turkish immigrants who have assimilated into the German culture, and Turkish immigrants who have not yet adapted to German culture, found varying serum carotenoid patterns depending on the nationality and cultural adaptation(33).Significant differences were lost when objective SCORAD instead of SCORAD index was used, in this study. These significant differences may be due to social and cultural differences related to the participants' symptoms. Translational studies on the effect of beta carotene in human AD patients should be carried, due to the encouraging results from animal studies. Varying results in dietary and serum carotenoids in human studies may be caused by differences in cultural, dietary habits, and affordability.

Significant differences in mean folate (Vitamin B9) intake between mild and severe groups were evident when participants were classified only according to Objective SCORAD and not SCORAD index. Significant differences between dietary intake of other types of Vitamin B and AD severity were not evident. Ito's study reported a lower dietary intake of folic acid (Vitamin B9) among AD patients. The difference was not statistically significant. Intake of Vitamin B3 (niacin) was significantly lower among the AD group than controls. Correlation between the various types of Vitamin B and SCORAD was significant only for Vitamin B6 (Pyridoxine) (3). The study by Ito et al. did not use the Objective SCORAD to discount the subjective components of patients' symptoms. Research on niacin intake and adult onset AD among women in the United States of America concluded that niacin intake was not protective in the developing AD in adulthood

(37). This study also reported an increased risk of AD with supplementary B complex and multivitamin intake. Only a food frequency questionnaire (FFQ) was used in this study, a method that was not superior to repetitive dietary recall (38,39) or a blended approach using both dietary recall and the FFQ (40). A study reported lower serum folic acid levels in AD patients than controls that were not statistically significant (41). Nottingham Severity Score was used to stratify the severity of AD cases. A systematic review concluded that only SCORAD, Eczema Area and Severity Index (EASI), and Patient-oriented Eczema Measure (POEM) have been tested sufficiently and performed adequately as a measure of AD severity (42). Another study found that serum folate levels were inversely associated with high total IgE levels, and atopy (43).

Ito et al. found that omega 6 –polyunsaturated fatty acids (n-6 PUFA) intake was significantly higher in the mild AD group than the severe AD group (3). We found no such association for n-6 PUFA in our study. Many studies revolving around the dietary intake of fatty acids inflammatory skin conditions are on PUFAs where many of the lipid mediators that regulate inflammation are metabolites derived from omega-6 (n-6 PUFA) or omega-3 (n-3 PUFA) fatty acids. The relationship between these PUFAs and inflammatory skin conditions is complex. In general, n-6 PUFAs are associated with pro-inflammatory responses, while n-3 PUFAs are associated with anti-inflammatory responses (44). Severe AD patients would have expected to have a higher intake of n-6 PUFA than mild AD patients. Similarly, SFA is pro-inflammatory and has been implicated in many non-communicable diseases.

In our study, total fat and saturated fatty acid (SFA) intake among mild AD participants were significantly higher compared to the severe AD group when they were classified under objective SCORAD. Though we know that SFA an integral component of lipids found in the stratum corneum, we have not come across any explanation in the literature on how dietary saturated fat affects the outcome of AD. Lipids in the stratum corneum are highly specialized. The major constituents of these lipids are composed of ceramides, free fatty acids, and cholesterol in an approximately 1:1:1 molar ratio (45).The free fatty acids in the skin barrier are usually saturated, unbranched and usually 14-34 carbons long. Similar saturated, unbranched free fatty acids are also an integral part of the sphingoid base that is the backbone of ceramides (46).

In assessing food preferences we looked at only the mild and severe AD participants as these were the two extreme ends of the disease spectrum, and any changes in food preferences would be evident. Vegetable and fruit intake among adult Malaysians has been low. Between 2000-2002 and 2005-2007, the average daily consumption of vegetable and fruit among Malaysians was 109 g for vegetables and 152 g for fruits (261 g total). The combined daily vegetable and fruit intake of Malaysians is far below the WHO's recommendation for optimal health (47). Fruits consumed by mild AD participants were similar to those consumed by the general Malaysian public. Apple, banana, orange, watermelon, and papaya were the top five fruits consumed by Malaysians in general (48). The four popular leafy vegetables consumed by Malaysians were cabbage, chinese mustard leaves, swamp cabbage, and spinach (48). Again, vegetable consumption among the mild AD group was similar to that of the general Malaysian population, with differences seen among those with severe AD. Limitations of this study in investigating food preferences and avoidances are known. Research on food preferences and avoidances is worthy of a separate, more focused study in the future. Carrots classified as "roots and tubers" were the second most consumed vegetable after potato among Malaysians (48).

Poultry meat recorded the highest per capita consumption (PCC) of 52.0 kilogrammes per year followed by chicken/duck egg (22.2 kg/year), pork (16.3 kg/year), and beef (5.6kg/year) (49). No deductions could be made from our study, as poultry meat (chicken) was the main intake of meat for both mild and severe AD participants.

PCC of mackerel (5.2 kg/year) was the highest among other seafood followed by shrimp (3.9 kg/year), tuna (2.5 kg/year), cuttlefish (kg/year), and crab (0.4kg/year) (49). Mackerels popularly consumed in Malaysia consist of the spanish mackerel (tenggiri) and the indian mackerel (kembung). Both mild and severe AD participants consumed mackerels. The glaring difference noted between these two groups was that none of the severe AD participants consumed prawns and anchovies, while anchovies were, in fact, the most consumed seafood among mild AD participants. These findings correspond with the reported food avoidance of certain seafood, predominantly in the crustacean and mollusk groups. Consumption of these foods usually caused pruritus and flares of AD.

Food allergies are typically type I hypersensitivity reactions. They can also present as type IV hypersensitivity reactions involving food antigen-specific T-cell responses that can damage the gut mucosa, as seen in celiac disease and food protein-induced enterocolitis. None of the participants had typical type I hypersensitivity reactions. Examples of type I hypersensitivity reactions are anaphylaxis, urticarial, angioedema, nor pulmonary reactions. There were also no type IV hypersensitivity reactions. Some patients claimed that the mentioned food triggers that worsened AD had varying effects, worse if foods were not fresh (foods stored over a long period). These were foods that contained histidine. We postulate that the conversion of histidine to histamine by histamine-producing bacteria (HPB) may be the trigger

for worsening AD. Examples of HPB are Photobacterium phosphoreum and Raoultellaplanticola (50). These bacteria possess histidine decarboxylase that facilitates this conversion.

This study had clear limitations in addressing food preferences and avoidance. Food preferences and avoidance in a population with an inflammatory condition like AD requires a specific study design. The study design should incorporate all the relevant features in a validated research tool. Such attributes were beyond the scope of this study. It is an important aspect worthy of a separate, more focused, study. A food avoidance and symptom questionnaire would have been able to show an association and a validated FFQ would have been useful in a larger sample to identify dietary pattern. Principal component analysis (PCA) (51) and cluster analysis can be used to study dietary pattern, both of which was beyond the scope of this study.

CONCLUSION

SCORAD index and objective SCORAD were strongly correlated, ($r=0.985$; $n=62$; $p<0.001$), yet significant differences in means, except for magnesium, was lost when AD was stratified using objective SCORAD. Subjective symptoms of the patients may have played a role in these changes. Social and cultural differences related to the participants' symptoms may have also contributed to these changes. A large portion of under reporters may be due to reduced nutrient intake during AD flares. Findings from this study would help plan more extensive research in the future. Examples being, the role of magnesium in AD severity, and the effect that conversion of histidine to histamine in food has on aggravating AD being good examples. Planning an efficient case-control study looking into dietary risk factors in AD would also be a worthy endeavor.

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