Fasting blood glucose and insulin are not associated with atopic dermatitis in a pediatric population: A longitudinal cohort study from the Avon Longitudinal Study of Parents and Children

To the Editor: Early identification and management of children at high-risk of diabetes is instrumental in preventing complications in adulthood.[1] Atopic dermatitis (AD) is one of the most common chronic childhood conditions and may be associated with diabetes because of (1) inflammatory processes involving insulin-driven increases in adipokines that worsen AD and (2) increased insulin resistance due to systemic inflammation from AD.[2,3] Therefore, it is important to understand whether children with AD would benefit from diabetes risk assessment and treatment. While some prior studies found a positive association between childhood AD and diabetes, others found a negative association or no association at all, and most have not assessed AD severity or biomarkers.[4,5]

Our study aims to determine the extent to which AD activity and severity are associated with fasting blood glucose and insulin in late childhood and adolescence. We performed a secondary analysis of the Avon Longitudinal Study of Parents and Children cohort, an ongoing longitudinal birth cohort from Avon, England. The study website contains additional details: http://www.bristol.ac.uk/alspac/researchers/our-data/. We included children with AD data at ages 9, 15, and/or 17 (n = 9067). Using AD activity and severity as the exposure and fasting glucose and insulin levels as the outcomes, we performed cross-sectional analyses at ages 9, 15, and 17 using logistic regression models. AD activity was based on a maternal- or self-reported questionnaire that asked about disease activity and severity over the past 12 months. AD severity was categorized as "no problem/mild" and "moderate/severe." Glucose measurements at age 9 were limited to a random sample of participants as part of a substudy (n = 851), while all participants were invited to participate in the glucose measurements at ages 15 and 17. High fasting glucose was defined as ≥5.6 mmol/L based on the International Diabetes Federation guidelines. Since insulin is not included as a diagnostic measure for diabetes in the International Diabetes Federation consensus, we used a cut-off of those who have values equal to or over the 90th percentile in the cohort to indicate being at risk.

The study population were half female (50.85%) and mostly White (95.98%). The annual period prevalence of active AD ranged from 14.45% at age 15 to 18.82% at age 9 (Table I). We did not find significant associations between AD and blood glucose at any time point, and there did not appear to be consistent trends by severity. However, we did find a significant positive association between moderate/severe AD and insulin levels at age 15 (Fig 1). Linear models using log-transformed continuous blood values and complete case analysis designed to address missing data concerns showed similar results (Supplementary Tables, available via Mendeley at https://data.mendeley.com/datasets/bxhvcftyns/1). Our study was limited by a single blood value per participant at each time point, which may not be an accurate reflection of the participant's average blood level. Moreover, as our cohort was predominantly White, these results should be tested in more diverse populations. The lack of consistent trends in our results, combined with mixed findings from prior studies, do not support a strong association between AD and fasting blood glucose.

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Table I. Cohort characteristics

Characteristic	9 y old *N* = 4457	%	15 y old *N* = 2394	%	17 y old *N* = 1644	%
BMI	4380	Mean (SD): 17.57 (2.76)	2367	Mean (SD): 21.43 (3.42)	1610	Mean (SD): 22.38 (3.51)
Cholesterol (mmol/L)	4135	Mean (SD): 4.28 (0.68)	2394	Mean (SD): 3.77 2(0.65)	1638	Mean (SD): 3.79 (0.68)
Sex	4457		2390		1643	
Female	2180	48.91	1340	56.07	983	59.83
Race	4161		2205		1527	
Non-White	155	3.73	82	3.72	52	3.41
Highest education of parent*	4210		2231		1545	
Vocational	197	4.68	74	3.32	46	2.98
O level/CSE	1337	31.46	598	26.80	382	24.72
A level	1473	34.99	805	36.08	536	34.69
Degree	1203	28.57	754	33.80	581	37.61
Mother had diabetes	4190		2219		1534	
Yes	39	0.93	19	0.86	17	1.11
Mother had AD	4457		2394		1644	
Yes	1009	22.64	598	24.98	382	23.24
Social class†	4140		2198		1516	
Professional	714	17.25	459	20.88	351	23.15
Managerial and technical	2016	48.70	1084	49.32	761	50.2
Skilled nonmanual	983	23.74	468	21.29	285	18.8
Skilled manual	290	7.00	127	5.78	80	5.28
Partly skilled	120	2.90	51	2.32	35	2.31
Unskilled	17	0.41	9	0.41	<5	<0.5
Exposures						
Current active AD	839	18.82	346	14.45	242	14.72
Definite, no prob/mild	632	14.18	198	8.27	N/A	N/A
Definite, mod/severe	206	4.62	148	6.18	N/A	N/A
Outcomes						
Glucose (mmol/L)	810	Mean (SD): 4.95 (0.40)	2394	Mean (SD): 5.20 (0.37)	1638	Mean (SD): 5.01 (0.49)
High glucose (fasting: ≥5.6 mmol/L)	53	6.54	242	10.11	88	5.37
Insulin (IU/L)	4196	Mean (SD): 11.52 (13.91)	2390	Mean (SD): 10.11 (5.69)	1610	Mean (SD): 7.95 (6.94)
High insulin‡	422	10.06	220	9.21	131	8.14

To reduce skewness, the glucose and insulin measurements were log-transformed for the purposes of analyses.
A, Advanced; *AD*, atopic dermatitis; *BMI*, body mass index; *CSE*, certificate of secondary education; *O*, ordinary.
*Based on British-based education levels. Vocational training is occupation-based training. O level represents 11 y of academic study and marks the end of the secondary education cycle. O level and CSE are equivalent. A level represents an additional 2 y of study (13 total) after the O level is obtained and is an admission requirement for university to pursue a degree.
†Based on highest parental occupation level at time of initial study enrollment.
‡High insulin (≥90th percentile insulin for each age group within cohort).

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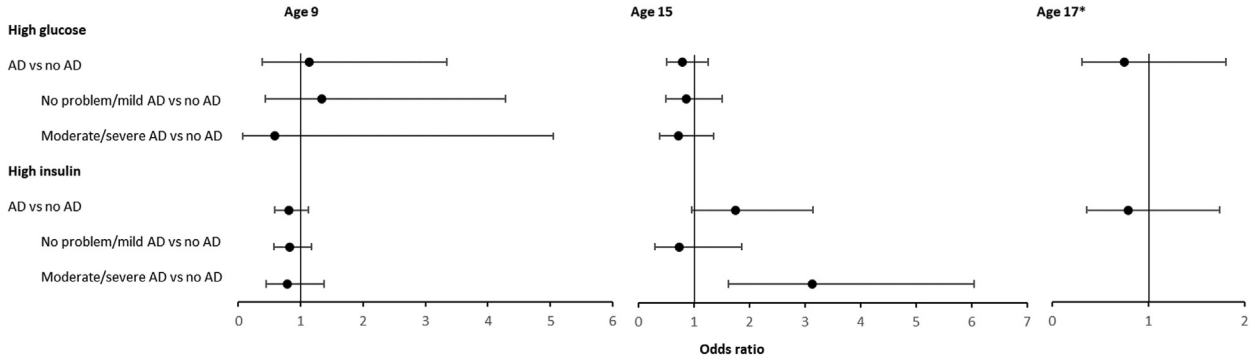

Fig 1. Adjusted odds of high glucose and insulin according to atopic dermatitis disease activity and severity. Logistic regression model was adjusted for sex, race, maternal delivery age, highest parental education level, social class assessed through parental occupation, body mass index, cholesterol, parental history of atopic dermatitis, and family history of diabetes. Sample sizes by age group are as follows: glucose analysis: age 9 ($n = 490$), age 15 ($n = 1992$), age 17 ($n = 1357$); insulin analysis: age 9 ($n = 3681$), age 15 ($n = 1995$), age 17 ($n = 1302$). 95% CIs are denoted by the error bars. *AD severity data were not captured at age 17. *AD*, Atopic dermatitis.

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Key words: ALSPAC; atopic dermatitis; biomarkers; clinical research; diabetes mellitus; endocrinology; epidemiology; pediatric dermatology.

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Conflicts of interest

Dr Abuabara is a consultant to Target RWE and receives research grants to her institution from Pfizer. Dr Langan is an investigator on the European Union Horizon 2020-funded BIOMAP Consortium (http://www.biomap-imi.eu/) but is not in receipt of industry funding. Author Shan, Author Ye, Dr Ku, and Dr McCulloch have no conflicts of interest to declare.

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