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Short Report

Skin pigmentation is inversely associated with insulin resistance in healthy Japanese women

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Abstract

Aim. – As a low-pigment skin type is prevalent in men and women with type 1 diabetes, it is possible that skin pigmentation may be associated with insulin resistance. This study aimed to cross-sectionally examine this association in healthy women.

Methods. – Study participants were 792 Japanese women who attended a health examination and were not taking any medication for diabetes. Skin pigmentation on the inner upper and lower arms and forehead was measured using a Mexameter® skin colorimeter, a narrow-band reflective spectrophotometer. Data are expressed as a melanin index, which quantifies melanin content. Fasting blood glucose and insulin levels were also measured, and homoeostasis model assessment for insulin resistance (HOMA-IR) scores were calculated. Information on medical history and lifestyle factors were obtained by a self-administered questionnaire, while data on sun exposure were collected through interviews. Plasma 25-hydroxyvitamin D levels were measured in a subsample of women ($n = 464$).

Results. – Melanin indices at the inner upper and lower arms were significantly and inversely associated with fasting insulin levels and HOMA-IR after controlling for age, body mass index, smoking status, indicators for rater effects, cumulative sun exposure and season at the time of measurement. Additional adjustment for plasma 25-hydroxyvitamin D levels did not alter the results.

Conclusion. – These data suggest that skin pigmentation is associated with insulin resistance, and encourage future studies into the potential role of melanin and related factors in glucose homoeostasis.

Keywords: Insulin resistance; Melanin; Skin pigmentation; Sun exposure; Vitamin D

1. Introduction

Some early studies reported that blue eyes and a low-pigment skin type are prevalent in people with type 1 diabetes (T1D) [1,2]. A recent study found that skin pigmentation measured on the foot was significantly lower in people with T1D than in controls [3]. In addition, skin pigmentation measured at the dorsal surface of the forearm was significantly and inversely associated with daily insulin dose in those with T1D [3]. There have been no studies of skin pigmentation in type 2 diabetes (T2D). However, as insulin resistance is a prominent feature not only in T2D, but also in T1D [4], skin pigmentation might be related to insulin resistance. Therefore, the present study measured the intensity of melanin pigmentation in the skin and examined its association with insulin resistance in healthy Japanese women.

The prevalence of diabetes has been increasing around the world, and Japan is one of the nations most affected by the diabetes epidemic. Because insulin resistance is associated with the risk of diabetes, it is worthwhile identifying the factors associated with insulin resistance. It has also been proposed that vitamin D may have beneficial effects on insulin resistance [5]. Therefore, an account has also been taken of the potential

Abbreviation: HOMA-IR, homoeostasis model assessment for insulin resistance.

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involvement of vitamin D status by measuring its levels in a subsample of women.

2. Subjects and methods

The present study was part of an earlier one designed to assess the relationships between lifestyle, environmental factors and women's health, as described previously [6]. Our subjects were women who took part in a medical health checkup programme provided by a general hospital in Gifu, Japan, between October 2003 and March 2006, including 1103 women (the response rate was 74.5%). The present study, however, was limited to 855 women who participated over the course of the programme, which included blood insulin and glucose measurements. Of these 855 women, those who used medications for diabetes ($n = 9$) or who had a collagen disease ($n = 11$) such as rheumatism and systemic lupus erythematosus were excluded from the present analyses. In addition, 14 women did not participate in the skin melanin measurements, and 30 women did not report their sun exposure on interviews. Thus, the final study population comprised 792 women, aged 20–74 years [mean 45.4 years, standard deviation (SD) 9.0]. Informed consent was obtained from each woman, and the study was approved by the ethics board of the Gifu University Graduate School of Medicine.

All participants responded to a questionnaire that sought information on demographic characteristics, lifestyle, and medical and reproductive histories during a visit for a health checkup. Height and weight were measured, and fasting blood samples were drawn at approximately 8:00 AM.

Data on sun exposure since age 13 were collected through face-to-face interviews, adopting the methods described by English et al. [7]. The women had to identify periods in their lives during which they had stable patterns of outdoor activity. More specifically, they were asked how many hours they generally spent outdoors in the sun at age 13 and how long (until what age) the habit had lasted. Weekday and weekend exposures were recorded separately. These questions were repeated for each successive age interval. From these data, the total time spent outdoors from age 13 until the day of the interview was estimated. Use of sunscreens was determined by one question, "How often did you usually wear sunscreen when you went out in the sun for 30 minutes or more during summer?" Use of sunscreens was ranked at three levels: never; less than half of the occasions; and more than half of the occasions.

Skin pigmentation was measured using a Mexameter® MX 16 skin colorimeter (C + K Electronic GmbH, Cologne, Germany). The device is a narrow-band reflectance spectrophotometer designed to quantify melanin and haemoglobin content [8]. Data are expressed as melanin and erythema indices. (This report here only includes data concerning the melanin index.) The index increases as the skin becomes more pigmented. Participants rested for about 15 min in a room before the skin measurements were taken. Any cosmetics present on the selected sites were removed by the investigators. Measurements on the right upper inner arm were taken to estimate constitutive (non-sun-exposed) skin pigmentation. Measurements on the forehead were taken to estimate facultative (sun-exposed) skin pigmentation, which consists of constitutive skin pigmentation plus tanning. Measurements from the inner sides of the right lower arms were also taken. Each site was measured three times, and the mean value calculated from these. All of these skin measurements and interviews were done by the same two investigators. The forehead and inside of the upper arm have often been selected to represent sun-exposed and non-exposed sites, respectively, in previous studies [9,10].

As part of the health examination, the participants' plasma glucose and insulin levels were measured by a glucose-oxidase method and double-antibody radioimmunoassay, respectively. Insulin resistance was estimated by homoeostasis model assessment for insulin resistance (HOMA-IR), using the approximated equation of Matthews et al. [11]. Measurements of 25-hydroxyvitamin D (25[OH]D) were restricted to 464 women who participated in hormone studies. These were premenopausal women who had regular menstrual cycles of < 40 days, and postmenopausal women who had been without a menstrual cycle over the previous 12 months or women aged ≥ 55 years who failed to report their menstrual status. Plasma samples were stored at −80 °C until needed for assay. Plasma 25(OH)D levels were measured by a chemiluminescence protein-binding assay method (LSI Medience Corporation, Tokyo, Japan). The interassay coefficient of variation was < 10.8%.

Linear regression analyses were used to examine the relationship between the melanin index at each site and plasma levels of glucose, insulin and HOMA-IR. Blood biomarkers were log-transformed to better approximate a normal distribution. Age, body mass index (BMI), smoking status, cumulative sun exposure, season at the time of measurement and indicators for rater effects were included as covariates in the model (Model 1). Among these covariates, smoking status was missing for two women; thus, they were categorized as one group and treated as a dummy variable. Plasma 25(OH)D levels were further included as a covariate for the subset of 464 women (Model 2). In addition, years of education, sunscreen use, and intakes of total energy, vitamin C and vitamin E were also included as covariates (Model 3). To assess whether any associations were modified by BMI, 25(OH)D level or cumulative sun exposure, models including their product terms with plasma levels of glucose, insulin and HOMA-IR were also used. BMI, 25(OH)D levels and cumulative sun exposure were treated as two-level categorical variables using medians as cutoff values. All statistical analyses were performed using SAS statistical software.

3. Results

The means (SD) of fasting plasma glucose levels, insulin levels and HOMA-IR were 5.0 (0.7), 45.8 (26.7) and 1.49 (0.95), respectively, in our 792 study women. The means (SD) of the melanin indices were 133.4 (31.1), 147.1 (33.4) and 168.6 (40.4) at the inner upper arm, inner lower arm and forehead, respectively. Six women showed fasting glucose levels ≥ 7.0 mmol/L.

Melanin indices for the skin on the inner upper and lower arms were significantly and inversely associated with HOMA-IR and plasma insulin levels in all women after controlling for covariates (Model 1; Table 1). Similar associations were observed for

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