# Normative Values for Electrochemical Skin Conductance Measurements for Quantitative Assessment of Sudomotor Function in Healthy Indian Adults

C. Shivaprasad, Amit Goel, Alice Vilier[1], Jean-Henri Calvet[1]

Department of Endocrinology, Vydehi Institute of Medical Sciences, Bengaluru, Karnataka, India, [1]Medical Division, Impeto Medical, Paris, France

## Abstract

**Context:** Electrochemical skin conductance (ESC) test is a widely accepted objective technique for quantitatively assessing sudomotor dysfunction, which is one of the earliest-detected neurophysiologic abnormalities in diabetic patients with distal symmetric polyneuropathy. **Aims:** This study aimed to provide normative data for ESC values among healthy Indian participants and assess the potential influence of age, sex, and body mass index (BMI) on ESC measurements. **Settings and Design:** A sample of 217 healthy participants aged 18–75 years were recruited and assessed for parameters including age, gender, BMI, and ESC measurements of the hands and feet. **Statistical Analysis Used:** The Shapiro–Wilk test was used to assess the normality of the data. Pearson's correlation was used to evaluate the association between age, gender, and BMI, and ESC measurements. **Results:** The mean age of the participants was 43.3 ± 13.2 years, and mean BMI was 26.0 ± 4.3 kg/m$^2$. Mean ESC for the hands and feet was 68.9 ± 13.1 and 71 ± 12.9 micro-Siemens, respectively, and there was a significant correlation between values from the right and left hands and feet ($r = 0.9$, $P < 0.0001$). A significant correlation was also observed between ESC measurements of the hands and feet ($r = 0.94$, $P < 0.0001$). ESC values of both hands and feet declined with age. A weak but significant inverse correlation between ESC and age was observed for the hands ($r = 0.02$, $P = 0.01$) and for the feet ($r = 0.12$, $P < 0.0001$). There was no significant difference in hand or feet ESC measurement between male and female participants. No significant correlation was observed between BMI and ESC of hands or feet. Only age was identified as a significant determinant of ESC on multivariate logistic regression analysis. **Conclusions:** Normative values for Indians are lower than that reported for Caucasians.

**Keywords:** Diabetic peripheral neuropathy, electrochemical skin conductance, normative data, sudomotor function

## Introduction

Diabetic peripheral neuropathy (DPN), a common and troublesome complication of type 2 diabetes, is associated with significant morbidity, impaired quality of life, and economic burden.[1] Distal symmetric polyneuropathy (DSP) is the most common clinical presentation of DPN.[2] The early diagnosis of DPN can result in the effective implementation of preventive measures and intensive glycemic control, leading to an improved quality of life and reduced morbidity.[3] Up to half of the patients with DPN are asymptomatic in the early stages, frequently resulting in delayed diagnoses.[4] DSP often affects nerve fibers in a length-dependent manner and often presents as painful neuropathy.[5] Alterations in the peripheral autonomic nervous system (ANS) function involving sympathetic C-fibers are the earliest features of DSP. Sweat glands are innervated by these small unmyelinated sympathetic nerve fibers, and loss of sudomotor function is one of the initial neurophysiologic abnormalities detectable in DSP.[6] Sudomotor function can be assessed by several methods; however, the absence of reliable, simple, quick, and quantitative methods of evaluating sweat-gland function has limited their widespread use.[7] The electrochemical skin conductance (ESC) test is a widely accepted noninvasive and objective method for quantification of sudomotor function.[8] The test is also simple and rapid,

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**Address for correspondence:** Dr. C. Shivaprasad, Department of Endocrinology, Vydehi Institute of Medical Sciences and Research Centre, #82, EPIP Area, Whitefield, Bengaluru - 560 066, Karnataka, India.
E-mail: shvprsd.c@gmail.com



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requiring <2 min for completion. The ESC test is based on the principle of an electrochemical reaction between the chloride-ions in sweat and the electrode plates in contact with the soles/palms and the results are reported as ESC values.[8,9]

The diagnostic utility of the ESC test in the early detection of DPN has been demonstrated in several clinical trials.[10-12] Sudomotor function has been shown to be influenced by factors such as age, ethnicity, and gender, and hence, ethnic-specific normative reference values have to be defined.[8] A recent study reported lower mean ESC values in Indian subjects as compared to Caucasian subjects.[13] However, the dataset was heterogeneous and involved data on Indian subjects from different studies. Hence, the aim of this study was to provide normative data for ESC values among healthy Indian adults and to determine the potential influence of age, gender, and body mass index (BMI) on ESC values.

## Subjects and Methods

### Sample and data collection

The study population comprised 217 healthy participants between the ages of 18 and 75 years. The participants included healthy relatives of outpatients of the Department of Endocrinology and paramedical staff of Vydehi Institute of Medical Sciences and Research Centre, Bengaluru. The present study was conducted between June and December 2016. The inclusion criteria were healthy participants aged 18–75 years and with BMI <25 kg/m$^2$. Participants with a history of alcohol abuse, impaired glucose tolerance, diabetes, symptoms of peripheral neuropathy, or other known causes of neuropathy were excluded. The participants were subjected to neurological examination including testing of reflexes and vibration perception threshold to ensure they had no neurological deficit.

ESC was measured using Sudoscan™ (Impeto Medical, Paris, France), a device designed for the accurate and quantitative assessment of sudomotor function. It is based on the principles of reverse iontophoresis and chronoamperometry.[14] Neither a specially trained technician nor specific participant preparation is required for this test. In this test, participants place their palms and soles on stainless steel electrodes throughout a 2-min testing period. Sweat gland density is highest in the palms and soles. A low voltage direct current is then applied to the plates to attract the sweat chloride ions. Electrochemical reaction ensues between chloride ions in the sweat and the stainless steel plate electrodes. ESC is calculated as the ratio between the current generated and the voltage of the applied direct current. ESC is expressed as microSiemens (μS), with distinct test results for the hands and feet, and values <60 μS are considered abnormal.

### Statistical analysis

The results for quantitative variables are expressed as mean ± standard deviation values. Data analysis was done using Statistical Analysis System (SAS) software version 9.4, (SAS Institute, Cary, NC, USA). The Shapiro–Wilk test was used to assess the normality of the data. Pearson's correlation was used to study the correlation between hand/feet ESC on the left and right sides and to evaluate the association between age, gender, and BMI and ESC measurements. Student's *t*-test was used to evaluate significant differences between the means and Mann–Whitney U-test was used to evaluate differences in ESC values between male and female participants. The confidence was set at 95% and differences with $P < 0.05$ were considered to be statistically significant.

## Results

Sudoscan was performed on all the participants without any untoward incident. The mean age of the participants was 43.3 ± 13.2 years, and mean BMI was 26.0 ± 4.3 kg/m$^2$. The male to female ratio was 2.7:1 [Table 1]. The mean vibration perception threshold value was 7.5 ± 0.3. The mean ESC values for the hands and feet were 68.9 ± 13.1 and 71 ± 12.9 μS, respectively. There was a significant correlation between the right and left values for the hands and feet ($r = 0.9$, $P < 0.0001$) [Figure 1]. A significant correlation was also observed between the ESC values for the hands and feet ($r = 0.94$, $P < 0.0001$) [Figure 2]. The Shapiro–Wilk test for normality was negative. Both hand and feet ESC values declined with increasing age. A weak but significant inverse association between ESC values and age was observed both for the hands ($r = 0.02$, $P = 0.01$) and for the feet ($r = 0.12$, $P < 0.0001$) in this cohort [Figure 3]. There was no significant difference in hand or feet ESC values between male and female participants (Mann–Whitney U-test). No significant correlation was observed between the BMI and ESC values of the hands and feet. In the multivariate logistic regression analysis, only age was found to be a significant determinant of ESC value.

## Discussion

The ESC test has emerged as a promising tool for the early detection of peripheral neuropathy. Specifically, ESC is a measure of the function of unmyelinated sympathetic C-fibers that are damaged or lost early in the course of DPN. ESC has been evaluated against other traditional measures of small fiber functions such as the quantitative sudomotor axon reflex test (QSART), quantitative sensory testing with the determination of thresholds for warmth and cold, vibration perception threshold, and intra-epidermal nerve fiber density.[14-17] A good correlation has been observed between these traditional measures and ESC. The advantages of ESC are that it is a simple, noninvasive, quick, objective, and quantitative technique.

We have performed this analysis on 217 healthy adults to derive normative data for Indians. This sample size ensures the reliability of the study results as a reflection of the population at large. An excellent symmetry was noted between the right- and left-sided values of ESC. No differences were observed in relation to BMI and gender. A slight decrease in ESC was noted with increasing age.

A previous study found considerably lower normal values for ESC in Indian, Chinese, and African-American participants in

**Table 1: Distribution of hands and feet electrochemical skin conductance in the population and according to age and gender**

| | Overall | Age decile (years) | | | |
|---|---|---|---|---|---|
| | | 18-29 | 30-39 | 40-49 | 50-69 |
| Whole population (*n*) | 217 | 36 | 62 | 46 | 73 |
| Age (years) | 43.1±12.9 | 25.6±3.1 | 34.9±2.8 | 44±3.2 | 58.2±5.9 |
| BMI (kg/m²) | 25.8±4.7 | 23±4.1 | 26.2±5.3 | 27.2±3.3 | 26±4.6 |
| ESC (µS) | | | | | |
| Hands | | | | | |
| Mean±SD | 71.5±46.5 | 73.2±10.8 | 68.4±13.5 | 73.6±13.1 | 65.3±10.9 |
| Median | 72 | 75 | 73 | 75 | 66 |
| 5th-95th percentile interval | 47-87 | 54-91 | 49-85 | 61-88 | 46-79 |
| Feet | | | | | |
| Mean±SD | 73.5±49.5 | 79.7±6.3 | 72.4±10.4 | 75.5±8.4 | 65.4±12.2 |
| Median | 74 | 80 | 74 | 77 | 67 |
| 5th-95th percentile interval | 50-86 | 70-91 | 50-86 | 57-89 | 39-84 |
| Female (*n*) | 59 | 10 | 13 | 9 | 27 |
| ESC (µS) | | | | | |
| Hands | | | | | |
| Mean±SD | 70.4±9.5 | 71.8±11.3 | 72.9±5.9 | 69±12.1 | 65.7±11.2 |
| Feet | | | | | |
| Mean±SD | 73.5±9.7 | 79.3±6.8 | 72.8±11.9 | 77.4±7.8 | 64.7±15.7 |
| Male (*n*) | 158 | 26 | 49 | 37 | 46 |
| ESC (µS) | | | | | |
| Hands | | | | | |
| Mean±SD | 68.9±13.4 | 74±9.7 | 67.7±14.6 | 74.6±13.1 | 63±12.9 |
| Feet | | | | | |
| Mean±SD | 71.4±11.7 | 79.7±5.7 | 73.3±9.7 | 73.7±8.9 | 62.1±15.3 |

*n* (%) for categorical variables, mean±SD for continuous variables. ESC: Electrochemical skin conductance, BMI: Body mass index, SD: Standard deviation

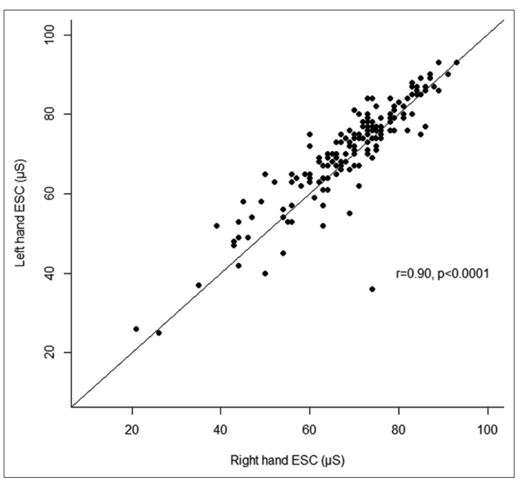


**Figure 1:** Correlation between the electrochemical skin conductance values of the left and right hands

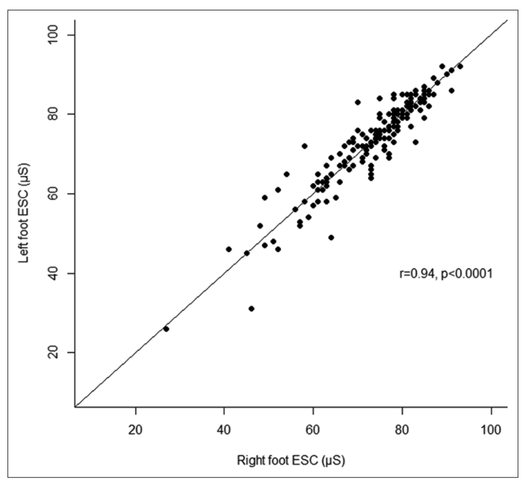


**Figure 2:** Correlation between the electrochemical skin conductance values of the left and right feet

comparison to Caucasian.[13] Our study validates these findings with respect to Indian participants and the ESC values in our study were similar to those previously reported. A larger sample size reduces the chances of potential influences with consequential discordant results. In addition, lack of apparent effect of sex and BMI on ESC results noted in our study was consistent with their observations. The exact reasons for ethnic variations in ESC remain to be elucidated; differences in secretory capacity, ion transport, or small nerve fiber properties could contribute to these variations. In line with the previous observation, age appeared to have a small but significant effect on ESC values, and ESC measurements declined with increasing age.[8,13] Sweat volume decreases with age, and the results of tests such as QSART dependent on sweat volume

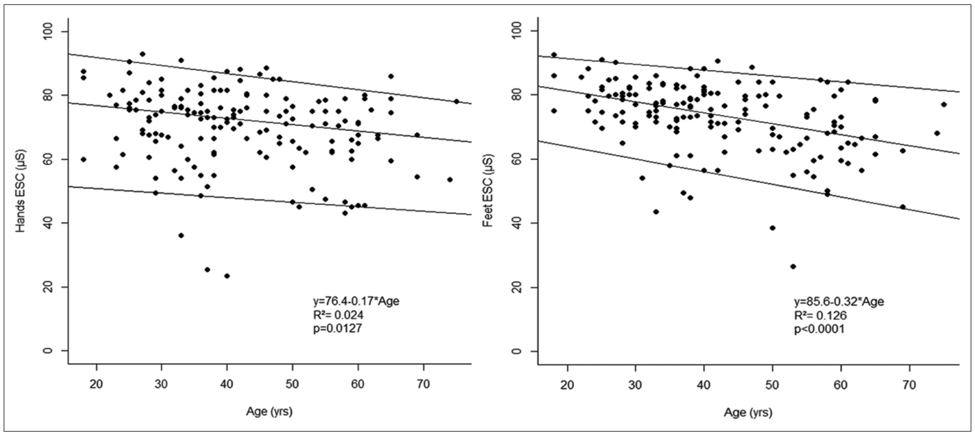


**Figure 3:** The evolution of electrochemical skin conductance of the hands and feet with age. Straight lines are 5th, 50th, and 95th percentiles, respectively

have been shown to decrease with age.[18,19] However, ESC values are not dependent on sweat volumes in contrast to QSART. Hence, age-related decline in autonomic function is the most probable explanation for this observation. Alterations in both parasympathetic and sympathetic components of ANS have been observed with age.[20-22]

The good symmetry observed between the left and right sides is superior to that reported by QSART.[23] In a previous study, ESC measurements in healthy children were found to be similar to those observed in healthy adults.[24] Good reproducibility has been reported between two sequential measurements performed at rest, and there is no significant variation in ESC after exercise.[13,25] These advantages make ESC an attractive option for large-scale screening and intervention trials.

The early detection of small peripheral fiber neuropathies requires an evaluation of sudomotor function. The traditional methods of assessing sudomotor function are technically complex and require rigid testing conditions. Limited accuracy, lack of widespread availability, and poor reproducibility are other limiting factors. ESC measurements compare very favorably against these validated sudomotor techniques and make it an attractive option for more widespread use. A limitation of this study was that only one measurement was performed per participant; however, the reproducibility of the measurements had already been evaluated previously.

## Conclusions

This study on healthy participants provides normative data of ESC measurements in Indians. We have also assessed the impact of age, gender, and BMI on ESC measurements. The normative data provided here will help in the interpretation of Sudoscan results.

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### Conflicts of interest

There are no conflicts of interest.

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