ABSTRACT

Diabetes Mellitus (DM) is a chronic metabolic disorder characterized by the hyperglycaemia with the disturbances of body metabolism resulting from the defects in insulin secretion, insulin action, or both. The chronic hyperglycaemia of diabetes is associated with the long term damage, dysfunction and failure of various vital organs like, the eyes, kidneys, nerves, heart and the blood vessels leading to micro and macro vascular complications.

DM is of two types, Type 1 accounting for 5% prevalence and Type 2 for 95% prevalence among the diabetic subjects. The health and economic consequences of this epidemic are huge and rising; the International Diabetes Federation estimated that the total number of people in India with diabetes was 65.1 million in the year 2013, and this may increase to 109 million by the year 2035; whereas, worldwide, nearly 382 million people have diabetes and this may increase to 592 million by the year 2035. In the present scenario, nearly 50% of the population were undiagnosed for the disease around the globe. Thereby, an early detection of the this disorder and its complications are utmost important, as nearly one third of the population were unaware of being developed into a diabetic individual by having one or more complications at the time of diagnosis.

The diagnosis of type 2 DM in the present state depend upon the blood sample extraction and this may lead to subject discomfort and possibility of infection when the procedure is repeated often. To overcome this difficulty, many researchers were involved in developing an alternative non-invasive diagnostic procedure but none was successful as on date as per the published original articles.
available in the Internet. Temperature is a vital and useful indicator of the various diseases. The skin surface temperature measurement could be made by various methods but the procedure should be non-invasive, risk free, relatively inexpensive and should produce highly accurate results.

The present research study aims to diagnose the type 2 DM based on the two different methodologies i) skin surface temperature as a non-invasive diagnostic marker in comparison with the standard bio-marker using infrared thermal imaging and ii) Quantitative estimation of HbA_{1c} (mmol/mol) that is present in the body through non-contact infrared thermogram and validation of the test results in comparison with the clinically obtained HbA_{1c}; thereby the non-invasively estimated HbA_{1c} could be used as a surrogate marker.

The present study was conducted based on the evidence that insulin has a profound impact on the cellular metabolism; diabetes and the core body temperature; the impact of the alteration of the core body temperature due to altered body metabolism was measured through non-contact skin surface temperature based on the standard practice of the European Academy of Thermology. There is a resurgence of interest in the application of infrared thermal imaging in medicine with improvements in the camera technology and the promise of the reduced costs. Thermograph captures the natural thermal radiation emitted by any object above absolute zero.

As per American diabetes association criteria, the threshold for diagnosis of diabetes was set as HbA_{1c} \geq 6.5\%. The total subjects (n=62) were studied out of which control (n=32) and diabetic subjects (n=30). IR camera was used to capture the
thermal images of the skin for the diagnosis of the disease; receiver operating characteristic (ROC) curve was used to set temperature (°C) as threshold for statistically significant body regions under t-test. Further, an optimal regression model was developed based on the skin surface temperature co-efficients of the body regions that exhibit a significant correlation with the clinically obtained HbA$_{1c}$ and the validation was performed against the bio-chemical assay.

The test results indicate that among the diabetic group, HbA$_{1c}$ indicated negative correlation with the carotid region \([r=-0.471, p<0.01]\) and the mean skin temperature was lower than the control group at the body regions namely knee \((p=0.002)\), tibia \((p=0.003)\), forehead \((p=0.014)\) and palm \((p=0.019)\). The palm region indicated the highest area under the curve of 0.711 (95% CI: 0.581-0.842) and the threshold was set as ≤33.85°C for diabetes, thereby sensitivity (90%) and specificity (56%) was obtained in determining the undiagnosed diabetes with positive predictive value of 65%, negative predictive value of 85% and accuracy of 73%.

Further, the optimal regression model \([r=0.643, p=0.000]\) was achieved to estimate the HbA$_{1c}$ without blood sample extraction and the validation was performed against the bio-chemical assay to indicate the sensitivity, specificity, positive predictive value, negative predictive value and with an accuracy of [90%, 55%, 65%, 85% and 72%] respectively. The paired t test for the bio-chemically measured HbA$_{1c}$ (54±21mmol/mol) and the non-invasively estimated HbA$_{1c}$ (54±14 mmol/mol) exhibits a positive correlation \([r=0.641, p=0.000]\) and the paired sample differences between the measured and the estimated HbA$_{1c}$ were not significant \([p=0.981; 95\%CI: -4.1 to 4.2]\).
The standard biomarker had diagnosed that subjects (n=19; 29) as pre-diabetic and the diabetic respectively; whereas, the IR thermography indicated subjects (n=13; 40) as pre-diabetic and diabetic respectively among the study group. The validation results indicate that the IR thermography had shown n=14 subjects as under false positive category; the further analysis based on the questionnaire indicate that (n=12) subjects were having a family history [DM: n=7; Cardiovascular disease: n=3; both (n=2)] and (n=2) with no history.

In conclusion, As HbA$_{1c}$ increases the skin surface temperature of the body decreases. The decrease in the skin surface temperature may be due to the decrease in the basal metabolic rate (BMR), poor blood perfusion and increased insulin resistance. Further, The non-invasive core body temperature measurement at the inner canthi of eye [$r$=-0.462, $p<0.01$] indicated negative correlation with HbA$_{1c}$, that signifies the early metabolic changes. Thereby, it indicates that the core body temperature also decreases with a decrease in the body metabolism. Thereby, a truly non-invasive infrared thermography could be used for obtaining the accurate HbA$_{1c}$ with no blood sample extraction; further, it could be used as a preferred diagnostic tool for type 2 diabetes. The cost effective screening program may aid in the earlier diagnosis and prevention of the disease and also to improve the outcomes in people who develop the condition, making the prevention and early detection of the disease an international public health priority.

The test results of the two different methodologies concluded the near similar accuracy; hence, the infrared thermography could be used as the preferred non-invasive surrogate tool for the prediction of pre-diabetes, type 2 diabetes and its complications.