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A CROSS-SECTIONAL, MULTICENTRE PILOT STUDY TO ASSESS THE EFFICACY OF INTELLIGENT HEALTH RISK ASSESSMENT (IHRA) SOFTWARE IN EARLY DETECTION OF TYPE II DIABETES MELLITUS, HYPERTENSION, DYSLIPIDEMIA

General Medicine

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ABSTRACT

Introduction: Type II Diabetes Mellitus (T2DM), HTN, and Dyslipidemia, are the leading causes of mortality and morbidity worldwide. IHRA (Intelligent Health Risk Assessment) offers a technological solution to enable early detection of these conditions and is expected to improve patient outcomes. Here, we have compared the specificity and sensitivity of IHRA risk scores against the gold standard methods. **Materials and Methods:** This cross-sectional, multi-centre, pilot study was conducted among both male and female study participants. Data on demographics, physical examination, laboratory investigations, and vital signs were recorded. Using a recommended infrared thermal imaging camera, a full one-minute video of the participant's face was taken and risk scores were calculated using IHRA software. **Results:** A total of 497 participants were included in the study. The ability of the IHRA derived risk score to predict T2DM was high [AUC = 0.88; p = 0.0001] with a sensitivity and specificity of 86% and 93% respectively. The ability of the IHRA derived risk score to predict hypertension was high [AUC = 0.84; p = 0.0001] with a sensitivity and specificity of 80% and 95% respectively. The ability of IHRA derived risk score to predict dyslipidemia was high [AUC = 0.77; p = 0.0001] with a sensitivity and specificity of 74% and 89% respectively. **Conclusion:** IHRA is an effective and reliable solution for the early detection of metabolic comorbidities. Nevertheless, further evaluation of IHRA in a larger population is required in strengthening the case to utilize it as a routine technique.

KEYWORDS

Type II Diabetes Mellitus (T2DM), Hypertension (HTN), Dyslipidemia, Risk score, Early detection, Computer vision, Signal processing, Infrared imaging

INTRODUCTION:

Type II Diabetes Mellitus (T2DM), Hypertension (HTN), and Dyslipidemia are the leading causes of mortality and morbidity worldwide. According to Wild et al.[1] globally, the prevalence of T2DM is predicted to double from 171 million in 2000 to 366 million in 2030 with the maximum increase in afflictions in India. It is predicted that by 2030 diabetes mellitus may afflict up to 79.4 million individuals in India, while China (42.3 million) and the United States (30.3 million) would also see a significant increase in those affected by the disease. Currently, an estimated 1.13 billion people worldwide have HTN.[2] WHO has set a global target to reduce the prevalence of the non-communicable diseases T2DM and HTN by 25% by 2025[3] (baseline 2010). The presence of T2DM, HTN and/or Dyslipidemia leads to other complications such as cardiovascular diseases, diabetic kidney disease and diabetic neuropathy.

Although biomarkers such as blood pressure, fasting blood sugar levels, HbA1C, serum adiponectin and inflammatory cytokines are being used by doctors for diagnosis and prevention of metabolic comorbidities, there is a need for the development of a procedure that is non-invasive, faster and makes it easy for periodic screening of individuals to identify those at an early stage before the disorder reaches clinically significant levels. Metabolic comorbidities such as T2DM, HTN and Dyslipidemia take a long time to manifest – estimated to be 4 to 7 years before these comorbidities can be detected by blood tests[4]. After any of these comorbidities afflict a person, the health and economic situation of a person is affected significantly.

In majority of the cases, these chronic illnesses are asymptomatic in nature or the symptoms are generic, leading to a delayed diagnosis. At present, there are no easy-to-use, accurate, non-contact and painless methods for early detection of these comorbidities. The existing solutions offer the diagnosis of one disease per device only, necessitating multiple tests. Due to this, the user is not opting for pre-diagnostic tests resulting in delayed care. However, it's important to note that these conditions are preventable if they are detected at an early stage.

Aarca Research, a health-tech company whose product IHRA[5] (Intelligent Health Risk Assessment) is a first-of-its-kind, pre-diagnostic method for the early detection of T2DM, HTN and Dyslipidemia. IHRA is an independent test that can be utilized in very early subclinical stages and long before the intended medical conditions can be clinically diagnosed using current methods like a blood test, or a blood pressure cuff.

Device description:

IHRA helps individuals of 21 years of age and older to learn about their health risks in relation to metabolic comorbidities. IHRA is a cloud-based software that uses computer vision, signal processing and machine learning models. IHRA takes non-contact infrared thermography video of the user's face as input, analyses and processes the said video and generates a report that provides risk scores for T2DM, HTN and Dyslipidemia. The risk is indicated on a scale of 0-10, with severity as Normal, very low, Low, Medium, High for each condition.

The physiologic principle used by infrared thermography is based on the heat generated by the cellular metabolism in the body. This generated heat is distributed by the blood and to the surface skin (which has a 0.98 emissivity), for loss by convection as infrared radiation. This radiation intensity and distribution are expected to be directly correlated to the physiological processes of circulation, micro perfusion, and ultimately metabolic activity[6]. In a healthy person, these processes are regulated to maintain a homeostatic balance and will be visible in uniform distribution of infrared radiation. In cases where blood supply is impaired or when a stimulus such as a disease occurs[7], it results in impairment in physiological processes. This causes homeostatic imbalance, and will be reflected in an irregular distribution of emitted infrared radiation.

The IHRA algorithm's primary principle is based on the analysis of the pulsatile nature of the blood flow through emitted infrared radiation and modelling its variability under the influence of T2DM, HTN and/or Dyslipidemia. To measure the pulsatile nature, IHRA uses a region of interest (ROI) consisting of superficial temporal arteries, which are part of external carotid arteries on an individual's forehead. The quasi-periodic pattern produced by the arterial blood flow can be measured from the infrared radiation around the skin in the vicinity of the superficial arteries[8]. As the blood vessels in the face and skull are coursing through very thin tissue (less than 5mm) between the bones of the skull and the skin covering the skull, they are readily and easily visualized with infrared imaging. For IHRA, an infrared video of

approximately one-minute duration of the ROI is taken from a recommended thermal camera manufacturer. This one-minute video produces nearly 3600 temporal infrared intensity points to build two signals in the time domain, permitting the real-time evaluation and its variability.

T2DM, HTN and Dyslipidemia by means of endothelial dysfunction, atherosclerosis or/and arterial stiffness, causes variations to the pulsatile nature of the blood flow and creates homeostatic imbalance and has been well researched [9-16]. Earlier studies of blood flow models have shown that atherosclerotic plaques preferentially develop in areas with low wall shear stress, such as at bifurcations or inner curves. Wall shear stress and stress inside the vessel wall may affect plaque formation and composition by causing alterations in the wall structure and metabolism creating a measurable relative difference [17-20]. IHRA's machine learning models determine these second-order differences in the observed blood flow parameters (Figure 1) in the superficial temporal arteries under the influence of T2DM, HTN, and Dyslipidemia, and estimate the risk by comparing it with previously identified relations in healthy and already diagnosed individuals. The report (Figure 2) visually highlights disease status in the form of a risk score and provides recommended next steps.

IHRA reports can help general practitioners and healthcare professionals to review and identify individuals who are showing early indications of the mentioned conditions, design and implement interventions such as enrolling individuals into coaching programs or lifestyle improvement before it becomes an irreversible condition. In this study, we have compared the specificity and sensitivity of IHRA risk scores at a cut-off value against the gold standard methods for diagnosis of T2DM, HTN, and Dyslipidemia.

MATERIALS & METHODS:

Study participants:

The study was conducted in two centres namely, MedStar Superspeciality Hospital, Bangalore, India and Excel Hospitals, Hyderabad, India. The study was approved by the Royal Pune Independent Ethics Committee on 15th June 2021 and 20th July 2021 respectively. The study was registered in the Clinical Trial Registry of India (CTRI/2021/08/035507). After obtaining written informed consent, this cross-sectional, multi-centre, pilot study was conducted among both male and female study participants aged between 21 to 65 years with a median of 39 years. We excluded the following groups of patients: (i) Patients with established coronary artery disease as detected by angiogram/TMT/ECG or patients with symptoms suggestive of ischemic heart disease. (ii) Patients with established T2DM, HTN, and Dyslipidemia. (iii) Female patients with gestational diabetes. (iv) Female patients who are pregnant at the time of screening. (v) Patients with diagnosed thyroid dysfunction. (vi) Patients with Type 1 diabetes. (vii) Patients with any other diagnosed chronic medical illnesses. (viii) Patients on systemic steroids within 2 weeks prior to the study. (ix) Patients on statins. (ix) Presence of any condition(s) (mental/physical) which seriously compromises the participant's ability to take part in this study.

Study procedure:

The participants were enrolled based on the inclusion/exclusion criteria and participant history. The participants were made to undergo a screening procedure to determine whether they are meeting the required inclusion and exclusion criteria. Data on demographics, physical examination and vital signs were recorded. Participants were assessed using infrared imaging and their risk scores were calculated using IHRA software. The participant's IHRA risk scores were assessed prior to blood sampling. All the participant's blood pressure measurements were taken during the vital sign assessment. Investigations for fasting plasma glucose (FPG) and oral glucose tolerance test (OGTT) values were conducted through intravenous blood glucose tests. Participants' earlier laboratory diagnostic results for lipids, conducted within the last 3 months to the enrolment date, were considered. In case of absence of the lab results, the participant's blood sample under fasting state was taken using venepuncture for lipid panel test.

Infrared Imaging Process:

Participants were asked to walk into the imaging screening room. Participants were asked to complete a patient registration form with details of their medical history, family history and lifestyle information in IHRA software. Participants were allowed to rest in this room where relative humidity and room temperature were controlled (to achieve equilibration of body temperature with the ambient temperature). They were asked to relax for 10-15 minutes before beginning the assessment to bring vitals to the resting state and also to ensure that there was no sweat on the participant's face and he/she was not panting. No parts of the Participants were in contact with any hot or cold sources. Only a minimum number of persons were allowed inside the room. Participants were kept away from any air convection sources. A thermally uniform backdrop with high emissivity was used to minimize unwanted IR radiations from the surroundings. In addition, the screening area is ensured to be free from lighting sources with significant IR emissions or has significant forced convective airflow, as they can cause thermal artifacts. Precautions had been taken to minimize the variables that might influence temperature measurement. A wall-mounted, air-conditioning unit provided the uniform temperature inside the room. The infrared thermal camera was positioned on a tripod one meter away from the subject. The FDA cleared FLIR E95 (Table 1) infrared imaging camera was used to obtain the infrared video for this study for optimum performance. A well-trained technician was operating the infrared camera. Participants were asked to stay still and keep the face straight while sitting in front of the infrared camera. As a precautionary measure, participants were instructed not to use any skin creams, sun-blocking or self-tanning agents before recording the infrared video. Participants were asked to remove artifacts like glasses, caps, headbands if they are covering the ROI. It was ensured that no hair is covering the ROI region. A full one-minute infrared video of the subject's face was recorded. A high-resolution colour video was provided in real-time, which can be viewed on a miniature screen provided within the camera. The video was captured and stored on a removable PC card. Upon completion of the screening, the video was uploaded to the IHRA software which was used to analyse the video and to generate the reports.

Statistical analysis:

Since no data were available for this product, no formal sample size calculation was done. Missing data points were treated as missing and no imputation was done. Continuous data were summarized as mean±standard deviation or median (Interquartile range). Categorical variables were presented with frequency and percentages. Receiver Operating Characteristic Curves (ROC) was plotted to predict the sensitivity and specificity for T2DM, HTN and Dyslipidemia. 95% confidence intervals were constructed for sensitivity and specificity based on different parameters. Pearson's correlation was done to study the relationship between IHRA score and related gold standard investigations. Positive predictive values and negative predictive values for pre-diagnosing T2DM, Hypertension and Dyslipidemia were calculated. Statistical analysis was done using a statistical package for the social sciences (SPSS) v16. A p-value < 0.05 was considered statistically significant.

RESULTS:

A total of (n=497) participants were included in the study including individuals who were at a higher risk of developing T2DM, HTN and Dyslipidemia. The median of the laboratory investigations FPG and OGTT investigations were as follows: 94 (84 - 104) mg/dL and 131 (112-142) mg/dL respectively. The median of the SBP and DBP were 121 (118-130) mm/hg and 82 (79-90) mm/hg respectively. The median of the laboratory investigations LDL and TC investigations were as follows: 95 (84 - 121) mg/dL and 170 (155-189) mg/dL respectively (Table 2). The IHRA derived scores for T2DM, HTN and Dyslipidemia were 3.5 (2.6-4.4), 2.6 (1.3-4.4) and 2.8 (1.5-3.8) respectively.

There was a moderate positive correlation between IHRA derived risk scores for diabetes and OGTT (r=0.45; p=0.0001) and FPG (r=0.51; p=0.0001). There was a moderate positive correlation between IHRA derived risk scores for Hypertension and SBP (r=0.39; p=0.0001) and DBP (r=0.30; p=0.0001). There was a moderate positive correlation between IHRA derived risk scores for Dyslipidemia and LDL (r=0.49; p=0.0001) and TC (r=0.49; p=0.0001). Moderate positive correlations were seen between IHRA derived scores for T2DM, HTN and dyslipidemia with PI's risk assessment VAS score (Table 3).

The ROC curve was plotted to predict the ability of IHRA derived scores in assessing the ability to predict T2DM, HTN and Dyslipidemia in the study participants. The ability of the IHRA derived risk score for T2DM to predict whether a person has T2DM was high [AUC = 0.88; p = 0.0001] with a sensitivity and specificity of 86% and

93% respectively taking OGTT>140 as gold standard test and IHRA T2DM cut-off risk score is >=4 (Figure 3). The positive predictive values and negative predictive values were 86% and 93% respectively. The ability of IHRA derived risk score for T2DM to predict whether a person has T2DM was high [AUC = 0.84; p = 0.0001] with a sensitivity and specificity of 85% and 82% respectively taking FBS>105 as gold standard test and when IHRA T2DM cut-off risk score is >=4. The positive predictive values and negative predictive values were 60% and 95% respectively. The ability of IHRA derived risk score for HTN to predict whether a person has HTN was high [AUC = 0.84; p = 0.0001] with a sensitivity and specificity of 80% and 95% respectively taking SBP>135 and DBP>90 as gold standard test and IHRA HTN cut-off risk score is >=5. The positive predictive values and negative predictive values were 78% and 95% respectively (Figure 4). The ability of IHRA derived risk score for Dyslipidemia to differentiate whether a person has Dyslipidemia was high [AUC = 0.77; p = 0.0001] with a sensitivity and specificity of 74% and 89% respectively taking LDL>100 and TC>200 as gold standard test and IHRA Dyslipidemia cut-off risk score is >=3. The positive predictive values and negative predictive values were 92% and 68% respectively (Figure 5).

DISCUSSION:

T2DM, HTN and Dyslipidemia are the leading causes of mortality and morbidity worldwide. Apart from being a chronic disorder, they are emerging as global epidemics. Even though there are several attempts were made for non-invasive glucose or lipid measurement using infrared (IR) spectroscopy, photoacoustic (PA) spectroscopy, Raman spectroscopy, fluorescence, optical coherence tomography (OCT), Terahertz (THz) spectroscopy, and microwave sensing, they failed to provide sensitivity and specificity required for clinical usage. [21-22] Earlier studies and technologies developed using infrared thermography had three noted problems. First, the infrared cameras that were used were able to only produce a signal of human infrared emissions that has low sensitivity. Second, the devices used in these studies were incorporating cryogenically cooled infrared detectors making their usage bulky and inconvenient. Third, the produced infrared images were analysed by humans causing errors while reading thermal intensity data. IHRA addressed all three problems. By taking infrared videos using FDA cleared infrared thermal cameras with high resolution and frame rate, IHRA software is able to obtain strong bio-signals with high reproducibility. Technology advancements in infrared sensors have also helped achieve this. By using computer vision and machine learning models for processing the video, IHRA is able to extract and track precise ROI across frames which contributed to the construction of these signals.

The present study is the first trial done in the Indian population and to the best of our knowledge globally, that evaluated the use of non-invasive infrared imaging to identify individuals showing early indications of developing T2DM, HTN and Dyslipidemia. This study has demonstrated high efficacy of IHRA to identify individuals with early indications of developing T2DM, HTN and Dyslipidemia. Our study demonstrated clinically significant sensitivity and specificity for all three conditions using IHRA derived scores at cut-off value in comparison to gold standard tests. Two similar studies were done in the Indian population using infrared imaging that could be used as a diagnostic tool for T2DM[23]. In another study, conducted on the Indian population, a computer-aided diagnostic (CADx) model was used for the diagnosis of HTN using variables derived from non-contact static and dynamic infrared imaging in comparison with the pulse wave velocity (PWV)-derived parameters. The study demonstrated that the IR thermogram alone gave an accuracy of 82% (and 85% after feature selection by PCA), whereas the accuracy using standard methods like variables derived from PWV was only 71.4% (with and without feature selection)[24]. However, the sample size in both studies was smaller with lower specificity and sensitivity. Hence, the present study is the largest one done in the Indian population which used an infrared screening method to identify individuals with early indications of developing T2DM, HTN and/or Dyslipidemia.

The presence of T2DM, HTN and Dyslipidemia lead to other complications such as cardiovascular diseases, diabetic kidney disease and diabetic neuropathy. Moreover, once an individual reaches such stages of complications, it is difficult to reverse the individual to a healthy state.[25] Even though there are gold standard tests such as FPG, OGTT, SBP, DBP, LDL and TC it may not be easy to implement these investigations in public places due to logistical challenges and that these tests do not provide early detection. IHRA fulfils this gap of lack of early-stage screening methods. The data obtained in this study is promising. IHRA could be implemented on a large scale to overcome the limitations of the existing gold standard tests. The presence of such tools helps conduct community screenings and health camps. Currently, the study has been conducted in the Indian population and is unlikely that the results could differ across ethnicities.

CONCLUSION:

Our study has shown that IHRA is an effective and reliable solution for the early detection of metabolic comorbidities such as T2DM, HTN and Dyslipidemia. IHRA is a novel application of computer vision, artificial intelligence and signal processing. It can be used as a screening tool for the early detection of the onset of these conditions and to inform the healthcare personnel for further investigations. IHRA has the potential for widespread improvement in clinical outcomes and for deployment in large public health programs across communities. We also note that IHRA seems to be an attractive solution in situations where it may not be feasible to collect blood samples or where the activity is constrained by low resources. Hence, further evaluation of IHRA in a larger population would go a long way in strengthening the case to utilize it as a routine technique for the early detection of T2DM, HTN and Dyslipidemia, and as a Point of Care (POC) screening tool.

Figure 1: A schematic representation of the process steps

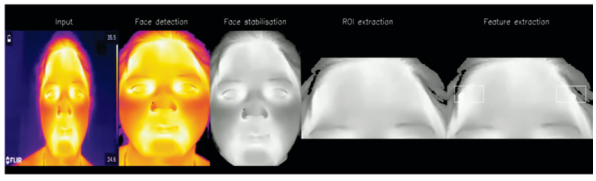

Figure 2: A sample user report generated from IHRA software

Figure 3: Sensitivity and specificity of IHRA to predict Type II Diabetes

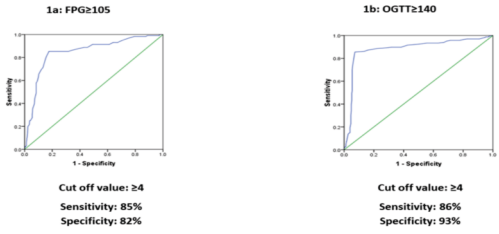

Figure 4: Sensitivity and specificity of IHRA to predict Hypertension

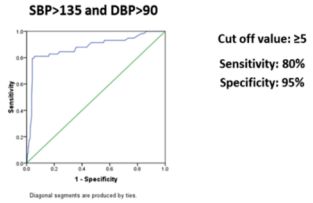

Figure 5: Sensitivity and specificity of IHRA to predict Dyslipidemia

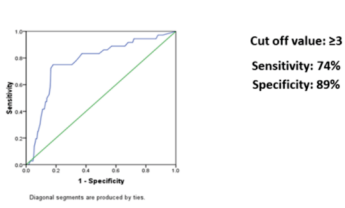

Table 1: Recommended infrared camera specifications:

Parameters	Specifications
IR Resolution (Minimum)	161,472 (464 x 348) pixels
Accuracy	±2°C (±3.6°F) or ±2% of reading for ambient temperature 15°C to 35°C (59°F to 95°F) and object temperature above 0°C (32°F)
Frames Per Second (FPS)	30
Field of view	24° × 18° (17 mm lens)
Object Temperature Range	–20 to +120°C (–4 to 248°F) 0–650°C (32–1200°F) 300–1500°C (572–2732°F)
Thermal Sensitivity/ NETD	<40 mK, 24° @ +30°C (+86°F)

Table 2: Baseline characteristics of study patients

Sl No.	Parameters	(N=497)
1.	DMI	3.5 (2.6-4.4)
2.	HTI	2.6 (1.3-4.4)
3.	DLI	2.8 (1.5-3.8)
4.	FPG, (mg/dL)	94 (84-104)
5.	OGTT, (mg/dL)	131 (112-142)
6.	SBP, (mm/Hg)	121 (118-130)
7.	DBP, (mm/Hg)	82 (79-90)
8.	TC, (mg/dL)	170 (155-186)
9.	TG, (mg/dL)	132 (106-147)
10.	HDL, (mg/dL)	40 (38-43)
11.	LDL, (mg/dL)	95 (84-121)
12.	VLDL, (mg/dL)	28 (25-32)

DBP: Diastolic blood pressure; DLI: Dyslipidemia index; DMI: Diabetes mellitus index; FPG: Fasting plasma glucose; HDL: High-density lipoprotein; HTI: Hypertension index; LDL: Low-density lipoprotein; OGTT: Oral glucose tolerance test; SBP: Systolic blood pressure; TC: Total cholesterol; TG: Triglycerides; VLDL: Very-low-density lipoprotein

Table 3: Correlation between IHRA risk score and other gold standard tests

Parameters			
IHRA derived Risk Score (Type II Diabetes Mellitus)	OGTT	FPG	PI's risk assessment VAS score
r value	0.45	0.51	0.15
p value	0.0001	0.0001	0.0001
IHRA derived Risk Score (Hypertension)	SBP	DBP	
r value	0.39	0.30	0.21
p value	0.0001	0.0001	0.0001
IHRA derived Risk Score (Dyslipidemia)	LDL	TC	
r value	0.49	0.49	0.11
p value	0.0001	0.0001	0.01

DBP: Diastolic blood pressure; FPG: Fasting Plasma Glucose; IHRA: Intelligent Health Risk Assessment; LDL: Low-density lipoprotein; OGTT: Oral Glucose Tolerance Test; SBP: Systolic blood pressure; TC: Total cholesterol; VAS: Visual analog scale

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