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RESEARCH ARTICLE

AN EVIDENCE BASED MINI-REVIEW OF ETHNIC DIFFERENCES IN BASELINE HOMA-IR VALUES

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ABSTRACT

The Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) has been a noninvasive tool used for decades to evaluate insulin resistance (IR) in clinical practice, as well as in large-scale, epidemiological studies. While standardized values have been established, we investigate whether HOMA-IR values fluctuate between different ethnic groups, and whether this has a direct impact on Systolic and Diastolic blood pressures. Thirty-nine studies were reviewed consisting of 68,965 total patients across 10 different ethnicities. A significant difference in HOMA-IR ranges were discovered between the ethnic groups, suggesting that this variable should be considered when using HOMA-IR to assess metabolic syndrome of insulin resistance and diabetes. Further investigation is needed to discover the underlying causes of these discrepancies and to more accurately identify HOMA-IR cut-off values for each ethnicity.

Key words: Insulin Resistance, Ethnic differences, HOMA values, Health Disparities, Personalized Treatment.

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INTRODUCTION

The Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) was developed by Matthews et al in 1985, as a method for assessing β-cell function and insulin resistance (Matthews, 1985). This method has been a useful epidemiological and clinical tool due to its favorable cost and simplicity compared to the gold standard euglycemic clamp (Greenfield, 1981). HOMA-IR is calculated by the following equation: Fasting insulin (microU/mL) x Fasting glucose (mmol/mL)) / 22.5. Numerous studies have validated HOMA-IR as a reliable surrogate measure of IR in humans.[3] However, as standardized reference rangeshave been estimated in the literature, studies have looked at how these ranges can fluctuate between different ethnic groups and bring its validity into question (Park, 2015). Recent publications regarding HOMA-IR has also delved into its possible connection to various conditions, such as microalbuminuria, post-liver transplant, pre-eclampsia, sleep apnea, and obesity (Park, 2015; Peplies, 2014; Lakhdar, 2014; Da Silva Alves, 2014; Abhari, 2014 and Iftikhar, 2015). A search for "HOMA-IR" on PubMed indicates the number of publications have been steadily increasing annually, from approximately 500 in 2010, to nearly 1000 in 2017. The focus on HOMA-IR in the literature highlights the importance of understanding how to more accurately evaluate HOMA-IR as a predictor of a patient's insulin resistance status. This review is aimed at evaluating the baseline values of HOMA-IR in different ethnicities, according to values found in the literature. Additionally, this study sought to determine the relationship between blood pressure and HOMA-IR in randomized adult populations, again, across different ethnic groups.

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MATERIALS AND METHODS

The literature was searched from 2008 to 2017 for publications related to the topic of HOMA-IR in adult populations, particularly with a focus on various ethnicities (Zhang, 2017; de Abreu, 2017; Kim, 2017 Lee, 2017; Zheng, 2017; Ekblad, 2017; Gaillard, 2016; Hossain, 2016; Yoon, 2016; Ling, 2016; Ahuja, 2015; Acton, 2015; Davis, 2015; Kurl, 2012; Lee, 2014; Zehsaz, 2014; Morimoto, 2014; Kang, 2014; Lee, 2014; Timóteo, 2014; Wu, 2013; Kim, 2013; Ghouri, 2013; Staimez, 2013; Furugen, 2012; Wongwananuruk, 2012; Yun, 2012; Deo, 2012; Mahadik, 2012; Chung, 2012; Yamada, 2012; Gao, 2012; Chung, 2012; Charles, 2011; Yamada, 2011; Kim, 2011; Zadeh-Vakili, 2011; Gupta, 2010; Esparza-Romero, 2010; Do, 2010; Ying, 2010; Esteghamati, 2007; Uzunlulu, 2009; Voruganti, 2008; Otsuka, 2008 and Sumner, 2008).

Table 1. Demographics of studies

Ethnicity	N	Gender (%)		HOMA-IR (Mean)	Systolic BP (Mean)	Diastolic BP (Mean)
		Male	Female			
African American	4,678	40	60	3.14	126.5	78.4
Brazilian	200	100	0	1.74	123.0	75.8
Caucasian	2,605	57	43	2.42	122.4	74.6
Chinese	11,829	40	60	1.65	128.8	74.1
Iranian	4,002	37	63	2.27	119.8	77.9
Japanese	15,748	57	43	1.40	119.0	74.1
Korean	24,588	35	65	1.97	118.7	76.0
Portuguese	1,784	51	49	1.10	--	--
South Asian*	2,492	37	63	2.26	125.9	83.4
Turkish	1,039	43	57	2.69	128.2	82.0
Total	68,965	44	56	1.89	121.8	75.9

*South Asian includes Indian, Pakistani, Bangaldeshi, or Sri Lankan origin

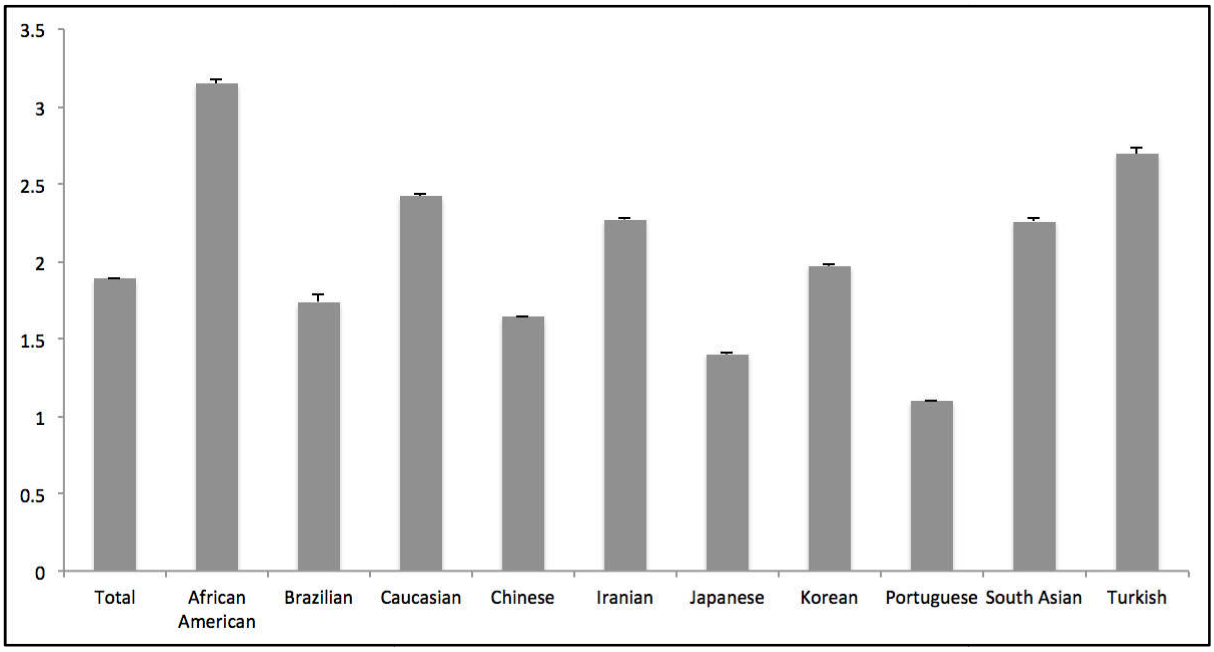

Figure 1. Baseline HOMA-IR Values for Adults of Different Ethnicities. Data presented as means ± SE.[11-56] Ten different ethnicities are represented with P-values below

Ethnicities			p-Value
Iranian	vs.	South Asian	p=1.000
Brazilian	vs.	Chinese	p=0.9324
All others			p<0.05

In addition to demographic information, baseline HOMA-IR values and systolic and diastolic blood pressure means were collected. The data is presented as mean ± standard error (SE) unless otherwise noted. The statistical significance of differences in baseline HOMA-IR values in the represented ethnic groups was tested using one-way ANOVA.

RESULTS

A total of 39 studies were reviewed, containing 68,965 adult patients, with 10 different ethnicities being represented. 30,345 (44%) of the patients were male. The average HOMA-IR for the entire population was 1.89±1.31 (Mean±Standard Deviation (SD)), with a range of means from 1.10 (Portuguese) to 3.15 (African American). HOMA-IR values with standard error are presented by separate ethnicities in Figure 1, as well as Table 1.All HOMA-IR values were significantly different ($p<0.05$) from one another, except for Iranian vs South Asian ($p=1.000$) and Brazilian vs Chinese ($p=0.9324$). Systolic and Diastolic Blood Pressure values were accumulated as well, and can be found with corresponding HOMA-IR values by ethnicity in Table 1. The average Systolic Blood Pressure for the entire population was 121.8±3.92 (Mean ±SD), with a range from 118.7 (Korean) to 128.8 (Chinese). The average Diastolic Blood Pressure for the entire population was 75.9±3.40 (Mean ±SD), with a range from 74.1 (Japanese) to 83.4 (South Asian). Pressures are plotted against HOMA-IR by ethnicity in Figures 2 and 3 for Systolic and Diastolic Blood Pressure respectively.

DISCUSSION

Insulin resistance (IR) is characterized by a lack of physiological response of the peripheral tissues – muscle, liver, adipose tissue - to the action of insulin. It is classically defined as impaired sensitivity to insulin mediated glucose disposal (Reaven, 2004). Several studies exist that demonstrate some ethnicities are more at risk of developing insulin resistance than other ethnicities (Srinivasan, 2000; Goran, 2002; Solano, 2003 and Albu, 2005). Furthermore, studies indicate that IR may play a role in the pathogenesis of cardiovascular disease (CVD), as insulin possesses a variety of antiatherogenic effects (Karamitsos, 2011 and Stein, 2007).

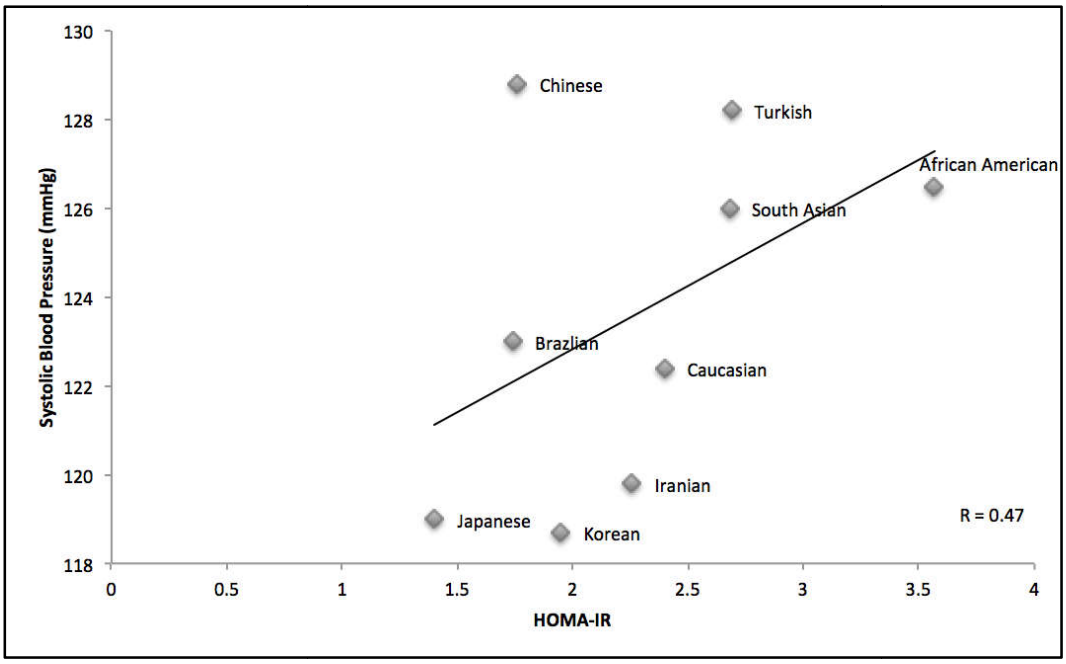

Figure 2. Baseline HOMA-IR and Systolic Blood Pressure in Ethnic Groups. [11-56]
Nine different ethnicities are represented with Trendline, R=0.47

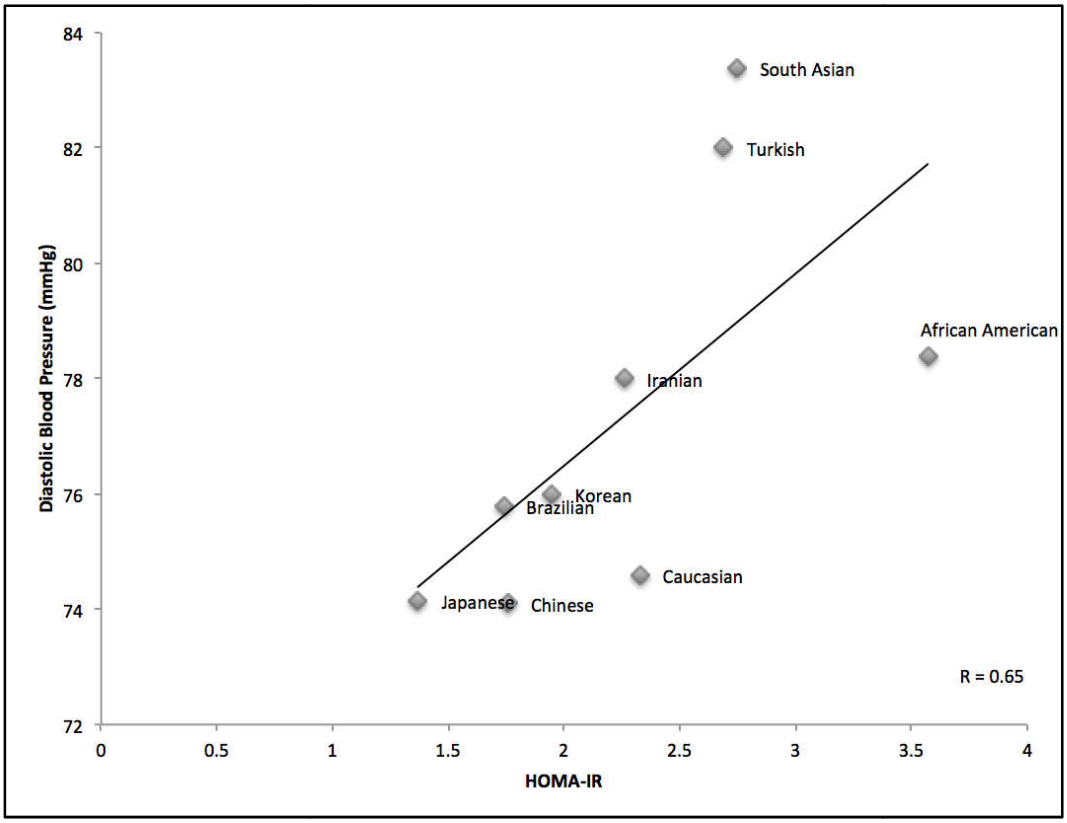

Figure 3. Baseline HOMA-IR and Diastolic Blood Pressure in Ethnic Groups.[11-56] **Nine different ethnicities are represented with Trendline, R=0.65**

Therefore, minority populations are at an increased risk of developing not only Type 2 Diabetes Mellitus (T2DM), but also CVD. While oral glucose tests are commonly used clinically to diagnose T2DM, they are not used to specifically detect insulin resistance. IR is instead typically measured by the hyperinsulinemic euglycemic clamp or an insulin suppression test (Tam, 2012), Park (2015) reviewed alternative options, such as biomarkers, that could change the way insulin resistance is detected (Park, 2015).

Some of the biomarkers reviewed include adiponectin, RBP4, chemerin, A-FABP, FGF21, fetuin-A, myostatin, IL-g, and irisin. Park et al acknowledge that a single biomarker may not be able to overcome the variable pathogenesis of insulin resistance, but offers that combinations of certain biomarkers may provide a more consistent, reliable method to accurately measure IR. Triglyceride levels have also been studied as a diagnostic tool in detecting insulin resistance across ethnic groups in young adults, however there are even studies

suggesting that triglyceride levels may not be a consistent indicator of insulin resistance among different ethnic groups (Sumner, 2008 and Otsuka, 2007). As advances are made in genomic and microbiome sciences, future tools may surface offering providers with a greater arsenal to quantify IR more accurately. Many studies have found that HOMA-IR is helpfulin measuring IRand decision making in high-risk patients, however, normal values may vary for ethnicity to ethnicity (Eslam, 2011). For instance, a study conducted by Qu et al (2011) revealed that the range of normal HOMA-IR might be higher in a healthy Hispanic population than for Caucasians (Qu, 2011), Ethnic variations such as these can complicate the utilization of HOMA-IR in clinical and population applications. It is also known that cardiovascular disease and insulin resistance are linked through overlapping pathophysiology. This heightens the importance of screening of high-risk patients for IR in order to reduce the risk of cardiovascular complications. As depicted in Figures 2 and 3, there was a moderate correlation between HOMA-IR and both Systolic (R=0.47) and Diastolic (R=0.65) blood pressures. This indicates that while there is certainly a connection between IR and CVD, that other factors mayinfluence this link and that HOMA-IR may not be a useful, independent predictor of CVD since IR is impacted by a myriad of factors, from aging and obesity, to socioeconomic status (Lawlor, 2002). While HOMA-IR is undoubtedly a valuable tool in clinical application, ethnic differences must be accounted for when measuring normal values before correlating these values into clinical decisions. As disparities in healthcare continue to pose challenges, it is important that providers are cognizant of potential discrepancies in lab values across different ethnicities. The importance of this issue is highlighted in this arena as T2DM is rapidly increasing across the world (Tang, 2015). Being aware of the respective HOMA-IR normal values can help providers more accurately diagnose and manage patients with insulin resistance. Further investigation into specific values for each ethnicity is warranted and can help with these efforts even further.

Conclusion

Data in the literature show that HOMA-IR significantly varies between ethnicities, and should be accounted for when using HOMA-IR as an indicator of insulin resistance. What is believed to be the normal lab range for HOMA-IR may not represent normal values for each respective ethnic group. Randomized, controlled studies are warranted to investigate the link between ethnicities and their HOMA-IR values, and define more accurate cut off values for each ethnic group.

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