

SPECIFIC COMMENTS TO AUTHORS

This manuscript is well designed and well written. However, the topic is not so novel due to too complex of factors associated with IR. And, they did not show definite therapeutic measures and possible progress in this topic, since these are more clinically significant.

Response: I extend my gratitude to the reviewer for their meticulous evaluation of the manuscript and their adept commentary, as well as their encouraging feedback. With these revisions, we aspire to have aligned the manuscript more closely with your expectations.

We added information in introduction regarding the therapeutic measures and possible progress in this topic, since these are more clinically significant as you suggested:

“Diet, lifestyle, and inflammatory cytokines all have major effects on insulin resistance. Currently, insulin sensitizers and lifestyle alterations are essential for managing and treating this illness. The use of insulin receptor cascade regulators and fresh perspectives on the prevention and treatment of primary IR are examples of future therapeutic targets. However, new discoveries have led to an improved understanding of insulin signaling and the mechanisms underlying insulin resistance. Additionally, sedentary lifestyles, high-fat and refined carbohydrate diets, and inflammatory cytokines have all been connected to IR ^[12-14]. Among the endocrine disorders associated with this illness are obesity, type 2 diabetes, hypercholesterolemia, hypertriglyceridemia, and arterial hypertension ^[12]. An ideal lifestyle and, in the case of obesity, weight loss are the most crucial treatment components ^[14,15]. For instance, it has been clinically demonstrated that metformin causes insulin sensitization in high-risk individuals. With the use of laboratory concepts related to insulin and glucose, the disease was discovered and confirmed to be a significant entity in metabolism. This work is currently being conducted and put into practice ^[16]. Research has investigated the relationship between IR and the development of cardiometabolic disorders ^[17,18]. Realistic therapeutic targets were identified after a thorough analysis of insulin signaling and IR mechanisms ^[19].”

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Since the authors have made some revisions in this edition, I have no other comment.

This manuscript may be meaningful for further research by providing some hints relevant of relationship between IR and NAFLD.

Thank you.