INPLASY PROTOCOL

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Corresponding author:
Mohammad Safiqul Islam

research_safiq@yahoo.com

Author Affiliation:
Noakhali Science and Technology University.

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None declared.

Effect of miR-196a2 rs11614913 polymorphism on cancer susceptibility: evidence from an updated meta-analysis

Aziz, MA[1]; Tahmina, A[2]; Islam, MS[3].

Review question / Objective: **MiR-196a2 rs11614913 polymorphism has been studied in a wide range of cancers throughout the years. Despite a large number of epidemiological studies performed in almost all ethnic populations, the contribution of this polymorphism in cancer risk is still inconclusive. Therefore, this updated meta-analysis was performed to estimate a meticulous correlation between miR-196a2 rs11614913 variant and cancer susceptibility.**
Condition being studied: **Different types of cancer patients and healthy controls were evaluated to detect the cancer risk in the individual case-control studies. We performed a meta analysis of these case control studies to get a pulled outcome risk.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 05 May 2022 and was last updated on 05 May 2022 (registration number INPLASY202250027).

INTRODUCTION

Review question / Objective: **MiR-196a2 rs11614913 polymorphism has been studied in a wide range of cancers throughout the years. Despite a large number of epidemiological studies performed in almost all ethnic populations, the contribution of this polymorphism in cancer risk is still inconclusive. Therefore, this updated meta-analysis was performed to estimate a meticulous correlation between miR-196a2 rs11614913 variant and cancer susceptibility.**

Rationale: **The MiR-196a2 rs11614913 polymorphism was found to be associated with different types of cancer. Some**

studies also found the opposite findings. As the finding is inconclusive, we conducted this meta-analysis to find a actual link between the rs11614913 polymorphism and cancer risk.

Condition being studied: Different types of cancer patients and healthy controls were evaluated to detect the cancer risk in the individual case-control studies. We performed a meta analysis of these case control studies to get a pulled outcome risk.

METHODS

Search strategy: An organized online article search was carried out using PubMed, ScienceDirect, EMBASE, Scopus, and Google Scholar databases to find all relevant literature using the following terms: miR-196a2, microRNA-196a2, miRNA-196-a2, miR-196a, 196a, rs11614913, single nucleotide polymorphism, SNP, variant, polymorphism, carcinoma, cancer, neoplasm, tumor, malignancy, either solely or in combination. For retrieving all possible publications, the reference list of the identified literature was also screened carefully. We did not implement any language restrictions in the literature search process. The search was limited to December 15, 2021.

Participant or population: Different types of cancer patients and healthy controls.

Intervention: Cases and controls were evaluated with respect to the presence of different genotypes. Association of polymorphism was detected as Odds ratio with 95% confidence interval.

Comparator: Different genotypes and allele frequency of cases were compared with controls.

Study designs to be included: Case control studies with the respective genotyping data of the mentioned SNP.

Eligibility criteria: Case control studies with the respective genotyping data of the mentioned SNP.

Information sources: PubMed, ScienceDirect, EMBASE, Scopus, and Google Scholar databases.

Main outcome(s): A total of 152 studies, including 120,135 subjects (53,818 patients and 66,317 controls), were included in this meta-analysis. Quantitative synthesis suggests that the miR-196a2 rs11614913 genetic variant is significantly correlated with the progression of overall cancer. Ethnicity-based subgroup analysis revealed a substantial link among the Asian population in the COD2, COD3, RM, and AM models. Stratified analysis based on the cancer types demonstrated a significant correlation with hepatocellular, lung, gynecological, oral, and renal cell cancer. Again, control population-based subgroup analysis reported a strong correlation for the HB population in the COD2, RM, and AM models. A substantial risk was also observed for other genotyping methods in multiple genetic models.

Quality assessment / Risk of bias analysis: No statistically substantial bias was reported in any genetic models that were confirmed by Egger's symmetric funnel plots and p-values of Begg-Mazumdar's assessment (p-values were found to be greater than 0.05 in every comparison). GRADE system was also used to detect the quality of the included studies.

Strategy of data synthesis: Dichotomous data will be synthesized to find the pulled odds ratio with a 95% confidence interval. Fixed effect and Random effect models will be utilized depending on heterogeneity.

Subgroup analysis: Different cancer types, ethnicities, genotyping methods and sources of controls.

Sensitivity analysis: A sensitivity analysis will be performed to evaluate the effect of individual studies on the polled outcomes.

Language: No language restriction was provided during literature searching.

Country(ies) involved: Bangladesh.

Keywords: MiRNAs; MiR-196a2; Cancer; Polymorphism; Meta-analysis.

Contributions of each author:

Author 1 - Md. Abdul Aziz - Author 1 searched studies, extracted information, wrote the primary draft.
Email: aziz.nstupharma@gmail.com
Author 2 - Tahmina Akter - Author 2 searched studies, extracted information, wrote the primary draft.
Email: tahmina.nstu65@gmail.com
Author 3 - Mohammad Safiqul Islam - Author 3 conceptualized and supervised the meta-analysis and critically reviewed and revised the manuscript.
Email: research_safiq@yahoo.com