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Brief Report

Opisthorchis viverrini-IgG antibody and proinflammatory cytokines IL-1β and TNF-α polymorphisms; synergy factor analysis

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Abstract

Cholangiocarcinoma is an important biliary tract cancer. This cancer is highly prevalent in Indochina. The opisthorchiasis, the *Opisthorchis viverrini* infection, is an important etiological factor for cholangiocarcinogenesis. The measurement of immune response, immunoglobulin G, is a way to monitor the intensity of infection, which can further imply the risk of cholangiocarcinoma. Regarding the disease severity, the role of genetic underlying factors including to proinflammatory cytokines polymorphisms, are mentioned for the important roles. There are some previous case controls studies to assess the odds ratio of the mentioned factors. Nevertheless, in real situation, there are usually complete multifactorial effects of several underlying factors. The synergistic effect due to multifactorial underlying etiologies is very interesting. Here, the authors performed synergy factor analysis for the combined *O. viverrini*-IgG antibody and to proinflammatory cytokines polymorphisms (IL-1β and TNF-α).

Keywords: Cholangiocarcinoma, Immunoglobulin, Interleukin, Tumor necrotic factor, Polymorphism, synergy

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Introduction

Cholangiocarcinoma is an important biliary tract cancer. This cancer is highly prevalent in Indochina. The opisthorchiasis, the *Opisthorchis viverrini* infection, is an important etiological factor for cholangiocarcinogenesis (1, 2). The measurement of immune response, immunoglobulin G, is a way to monitor the intensity of infection, which can further imply the risk of cholangiocarcinoma (3). Regarding the disease severity, the role of genetic underlying factors including to proinflammatory cytokines polymorphisms, are mentioned for the important roles (4,5). There are some previous case controls studies to assess the odds ratio of the mentioned factors. Nevertheless, in real situation, there are usually complete multifactorial effects of several underlying factors. The synergistic effect due to multifactorial underlying etiologies is very interesting.

Objectives

Here, the authors performed synergy factor analysis for the combined *O. viverrini*-IgG antibody and proinflammatory cytokines polymorphisms) [interleukin 1 beta (IL-1β) and tumor necrotic factor alpha (TNF-α)].

Core tip
The Opisthorchis viverrini infection, is an important etiological factor for cholangiocarcinogenesis.

Materials and Methods

The aim of this study is to assess the synergistic effect between *O. viverrini*-IgG antibody and to proinflammatory cytokines polymorphisms (IL-1β 511 and TNF-α 308) for cholangiocarcinoma risk. The primary published data for the risk analysis, odds ratio calculation, study for cholangiocarcinoma in endemic area, northeastern region of Thailand (6) are used for further mathematical modelling in the present study.

To assess the synergistic effect between *O. viverrini*-IgG antibody and to proinflammatory cytokines polymorphisms (IL-1β and TNF-α), the Synergy factor analysis according to the technique proposed by Cortina-Borja et al was done (7). For calculating, the synergy factor can be calculated according to this equation, "synergy factor = combine odds ratio for factor 1 and factor2/(odds ratio for factor 1 × odds ratio for factor 2)" (7). According to the referencing study (6), the odds ratio for *O. viverrini*-IgG antibody and to proinflammatory cytokines polymorphisms were

reappraised and used for further synergy factor analysis. The research followed the Tenets of the Declaration of Helsinki.

Results

The specific odds ratio for *O. viverrini*-IgG antibody and to proinflammatory cytokines polymorphisms are presented in Table 1. For the calculated synergy factors, the results are shown in Table 2.

Discussion

The cholangiocarcinoma is a biliary tract cancer with extremely prevalence in Southeast Asia. The liver fluke infestation is proven as an important risk factor for the cholangiocarcinogenesis (1,2). In the previous report, it is acceptable that the parasite act as a carcinogen (8). The high intensified infection, determined by OD *O. viverrini*-IgG antibody more than 0.24, is accepted as a risk (6). Regarding the host factor, the polymorphisms of IL and TNF are proven for relationship with risk of carcinogenesis.

Although there are many reports on those mentioned factors and risk of cholangiocarcinogenesis, there are few reports on the combined effect. In the recent publication by Promthet et al (6), there was an alteration of odd ratio when two combing factors were focused. Nevertheless, the exact synergistic effect is not assessed. In the present study, the synergistic factor analysis is done. According to the analysis, the degree of synergy is different and varied by the combination. This can confirm the complexity the underlying factor of both pathogen and host to the carcinogenesis process in liver fluke related cholangiocarcinoma development.

Authors' contribution

Both authors wrote the manuscript equally.

Table 1. The specific odds ratio for *O. viverrini*-IgG antibody and to proinflammatory cytokines polymorphisms according to the referencing data (6)

Focus background parameters	Odds ratio
High *O. viverrini*-IgG antibody	2.1
Low *O. viverrini*-IgG antibody	1.0
IL-1β CC Polymorphism	1.0
IL-1β CT Polymorphism	0.8
IL-1β TT Polymorphism	0.4
TNF GG Polymorphism	1.0
TNF GA Polymorphism	1.2
TNF AA Polymorphism	1.7
High *O. viverrini*-IgG antibody and IL-1β CC Polymorphism	2.5
High *O. viverrini*-IgG antibody and IL-1β CT Polymorphism	2.1
High *O. viverrini*-IgG antibody and IL-1β TT Polymorphism	1.1
Low *O. viverrini*-IgG antibody and IL-1β CC Polymorphism	1.0
Low *O. viverrini*-IgG antibody and IL-1β CT Polymorphism	0.9
Low *O. viverrini*-IgG antibody and IL-1β TT Polymorphism	0.9
High *O. viverrini*-IgG antibody and TNF GG Polymorphism	2.1
High *O. viverrini*-IgG antibody and TNF GA Polymorphism	2.4
High *O. viverrini*-IgG antibody and TNF AA Polymorphism	2.8
Low *O. viverrini*-IgG antibody and TNF GG Polymorphism	1.0
Low *O. viverrini*-IgG antibody and TNF GA Polymorphism	0.9
Low *O. viverrini*-IgG antibody and TNF A Polymorphism	2.2

Table 2. Synergy factor to assess the synergistic effect between *O. viverrini*-IgG antibody and to proinflammatory cytokines polymorphisms (IL-1β and TNF-α)

Focus background parameters	Synergistic factor
High *O. viverrini*-IgG antibody and IL-1β CC Polymorphism	1.19
High *O. viverrini*-IgG antibody and IL-1β CT Polymorphism	1.25
High *O. viverrini*-IgG antibody and IL-1β TT Polymorphism	1.31
Low *O. viverrini*-IgG antibody and IL-1β CC Polymorphism	0.48
Low *O. viverrini*-IgG antibody and IL-1β CT Polymorphism	1.13
Low *O. viverrini*-IgG antibody and IL-1β TT Polymorphism	2.25
High *O. viverrini*-IgG antibody and TNF GG Polymorphism	1.0
High *O. viverrini*-IgG antibody and TNF GA Polymorphism	0.95
High *O. viverrini*-IgG antibody and TNF AA Polymorphism	0.78
Low *O. viverrini*-IgG antibody and TNF GG Polymorphism	1.0
Low *O. viverrini*-IgG antibody and TNF GA Polymorphism	0.75
Low *O. viverrini*-IgG antibody and TNF AA Polymorphism	1.29

Conflict of interests

The authors declared no competing interests.

Ethical considerations

Ethical issues (including plagiarism, misconduct, data fabrication, falsification, double publication or submission, redundancy) have been completely observed by the authors.

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