



Review

Comorbid association of antiphospholipid antibodies and migraine: A systematic review and meta-analysis

Md. Asiful Islam^{a,1}, Fahmida Alam^{a,1}, Kah Keng Wong^{b,*}^a Human Genome Centre, School of Medical Sciences, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia^b Department of Immunology, School of Medical Sciences, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia

ARTICLE INFO

Article history:

Received 15 February 2017

Accepted 22 February 2017

Available online 7 March 2017

Keywords:

Antiphospholipid antibodies

Anticardiolipin antibodies

Anti-β₂-glycoprotein I antibodies

Lupus anticoagulant

Migraine

Meta-analysis

ABSTRACT

Background: Antiphospholipid antibodies (aPLs) namely anticardiolipin (aCL) antibody, anti-β₂-glycoprotein I (β₂GPI) antibody and lupus anticoagulant (LA) are autoantibodies produced against anionic phospholipids and proteins on plasma membranes. Migraine is a primary headache disorder which has growing evidences of autoimmune-mediated pathogenesis and previous studies suggested the presence of aPLs in migraine patients. **Aims:** The aim of this study was to evaluate the comorbid association between aPLs (aCL, anti-β₂GPI and LA) and migraine compared to healthy controls.

Methods: Studies were searched through PubMed, ISI Web of Science and Google Scholar databases without restricting the languages and year (up to October 2016) and were selected based on the inclusion criteria. Two authors independently extracted data from the included studies. All analyses were conducted by using random effects model to calculate the odds ratio (OR) and 95% confidence interval (CI). Quality assessment was carried out by using the modified Newcastle-Ottawa Scale (NOS). Publication bias was evaluated via visualization of funnel plots, Begg's and Egger's tests.

Results: The database searches produced 1995 articles, 13 of which were selected (912 migraineurs and 822 healthy controls). 8.59%, 15.21% and 4.11% of the migraineurs exhibited aCL, anti-β₂GPI and LA which was 4.83, 1.63 and 3.03 times higher, respectively, than healthy controls. A significant presence of aCL (OR: 3.55, 95% CI: 1.59–7.95; $p = 0.002$) or anti-β₂GPI antibodies (OR: 2.02, 95% CI: 1.20–3.42; $p = 0.008$) was observed in migraine patients, however, LA was not significantly associated (OR: 2.02, 95% CI: 0.50–8.37; $p = 0.320$). Majority of the studies ($n = 10$ of 13) demonstrated NOS score of 7 or above and no significant publication bias was observed.

Conclusion: Migraine might be an autoimmune-associated neurologic disorder. The presence of aCL or anti-β₂GPI antibodies was significant in migraine patients compared to healthy controls, suggesting an involvement of these autoantibodies in migraine attack.

© 2017 Elsevier B.V. All rights reserved.

Contents

1.	Introduction	513
2.	Methods	513
2.1.	Inclusion and exclusion criteria	513
2.1.1.	Types of studies	513
2.1.2.	Types of participants	513

Abbreviations: aCL, anticardiolipin; anti-β₂GPI, anti-β₂-glycoprotein I; aPLs, antiphospholipid antibodies; APS, antiphospholipid syndrome; BBB, blood-brain barrier; CGRP, calcitonin gene-related peptide; CI, confidence interval; DRVVT, dilute Russell's viper venom test; ICHD, International Classification of Headache Disorders; KCT, kaolin clotting time; LA, lupus anticoagulant; MeSH, Medical Subject Heading; MOOSE, Meta-analysis of Observational Studies in Epidemiology; NOS, Newcastle-Ottawa Scale; OR, odds ratio; PGE₂, prostaglandin E₂; RR, risk ratio; RVVT, Russell's viper venom time; SLE, systemic lupus erythematosus; T_c, T-Cytotoxic; T_h, T-helper; TNF-α, tumor necrosis factor-α; T_{reg}, T-regulatory.

* Corresponding author at: Department of Immunology, School of Medical Sciences, Health Campus, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia.

E-mail address: kahkeng@usm.my (K.K. Wong).

¹ Equal contributors.

2.2.	Search strategy	514
2.3.	Data collection and analysis	514
2.3.1.	Selection of studies	514
2.3.2.	Data extraction and management	514
2.3.3.	Assessment of heterogeneity and subgroup analysis.	514
2.3.4.	Quality assessment.	514
2.3.5.	Publication bias	515
2.3.6.	Statistical analyses	515
3.	Results	515
3.1.	Selection of studies.	515
3.2.	Characteristics of the included studies	515
3.3.	Association between aPLs and migraine by meta-analysis	516
3.3.1.	Anticardiolipin antibody	516
3.3.2.	Anti-β2-glycoprotein I antibody.	516
3.3.3.	Lupus anticoagulant	516
3.4.	Subgroup analyses	516
3.4.1.	Adult or pediatric	516
3.4.2.	Migraine with aura or without aura	516
3.5.	Quality assessment.	518
3.6.	Publication bias	518
3.7.	Heterogeneity	518
4.	Discussion	518
4.1.	Migraine and aPLs pathogenic relationships.	519
4.2.	Mediators of heterogeneity	520
4.3.	Limitations	520
4.4.	Future research	520
5.	Conclusion	520
	Funding.	520
	Conflict of interest	520
	Acknowledgments	520
Appendix A.	Search strategies employed for PubMed, ISI Web of Science and Google Scholar electronic databases	520
A.1.	PubMed.	520
A.2.	ISI Web of Science	520
A.3.	Google Scholar.	520
Appendix B.	L'Abbé plots for aCL and anti-β2GPI antibodies suggest no substantial heterogeneity, however studies assessing LA are suggestive of heterogeneity	521
Appendix C.	Supplementary data (MOOSE Checklist)	521
	References	521

1. Introduction

Antiphospholipid antibodies (aPLs) are a heterogeneous group of autoantibodies which react against anionic phospholipids and proteins on plasma membranes. Low titers of aPLs are observed in 1–5% of the healthy population, however, persistently high titers of aPLs [anticardiolipin (aCL), anti-β2-glycoprotein I (β2GPI) antibodies and lupus anticoagulant (LA)] have been observed in patients with antiphospholipid syndrome (APS) clinically presenting recurrent arterial, venous thrombosis and/or pregnancy morbidity [1–4]. High titers of aPLs were also observed in APS patients suffering from different neurologic disorders such as migraine, epilepsy, multiple sclerosis, cognitive impairment and dementia in which migraine has been the most frequently observed neurologic manifestations (up to 40%) [5].

Migraine is a primary recurrent headache disorder that affects approximately 18.5% of the world population [6], making the condition as one of the most disabling and costly medical complaints [7–9]. Although the complete pathogenesis of migraine attack is unclear, autoimmunity has been suggested recently to play a causative role in migraine pathogenesis [10,11]. Women are more susceptible to autoimmune disorders [12], likewise they are also more likely than men to be diagnosed with migraine [13]. Moreover, abnormal levels of several modulators of the immune system including CD4⁺ or CD8⁺ T cells, T-regulatory (T_{reg}) cells [11,14], tumor necrosis factor (TNF)-α [15] and prostaglandin E2 (PGE2) [16] have been observed in migraineurs particularly during the migraine attack phase. Martin et al. [17] observed that upon administration of immunotherapies, there is a decreased frequency [risk ratio (RR): 0.48] and disability (RR: 0.55) of migraine headache

in younger subjects (≤45 years of age), suggesting that autoimmunity modulation represents an avenue to treat migraine patients.

Several primary studies have investigated the comorbid association between migraine and the presence of aPLs. Although some of the studies reported the significant association of aPLs positivity with migraine [18,19], there were also studies that did not observe such relationship [20,21]. Therefore, the aim of this systematic review and meta-analysis was to identify the co-occurrence of aPLs in migraine patients compared to healthy subjects.

2. Methods

This meta-analysis was designed, implemented and reported based on the guidelines published by the Meta-analysis of Observational Studies in Epidemiology (MOOSE) group [22].

2.1. Inclusion and exclusion criteria

2.1.1. Types of studies

Prospective case-control studies published in any languages were included in which the presence or absence of aPLs (LA and/or aCL and/or anti-β2GPI antibodies) was reported in migraine patients compared to healthy controls. Studies published as review articles, case reports, clinical trials, editorials, letters and comments were excluded.

2.1.2. Types of participants

Migraine patients of any age, sex or race [without any underlying disorders including autoimmune diseases e.g., APS and systemic lupus

Download English Version:

<https://daneshyari.com/en/article/5665407>

Download Persian Version:

<https://daneshyari.com/article/5665407>

[Daneshyari.com](https://daneshyari.com)