Review

RISK FACTORS FOR CENTRAL SEROUS CHORIORETINOPATHY
A Systematic Review and Meta-Analysis

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Purpose: Central serous chorioretinopathy (CSC) is a common retina disease and has a relative high recurrence rate, etiology, and pathogenesis of which remains ambiguous. The systematic review and meta-analysis aimed to measure risk factors for CSC in a quantitative method, providing some precautions and interventions on this disease and preventing further recurrences.

Methods: A comprehensive literature review relating to risk factors for CSC through PubMed, Embase, Cochrane Library, China National Knowledge Infrastructure (CNKI), and VIP databases was conducted before March 2015. Odds ratio (OR) with 95% confidence interval (CI) was calculated after data combination to assess the associations between risk factors and CSC.

Results: A total of 9839 patients in 17 studies were included and risk factors with significant differences found between CSC and control groups were listed as follows: hypertension (OR = 1.7; 95% CI: 1.28–2.25), Helicobacter pylori (H. pylori) infection (OR = 3.12; 95% CI: 1.81–5.40), steroid usage (OR = 4.29; 95% CI: 2.01–9.15), sleeping disturbance (OR = 1.90; 95% CI: 1.28–1.83), autoimmune disease (OR = 3.44; 95% CI: 1.90–6.26), psychopharmacologic medication use (OR = 2.69; 95% CI: 1.63–4.45), and Type-A behavior (OR = 2.53; 95% CI: 1.08–5.96).

Conclusion: The authors concluded that hypertension, H. pylori infection, steroid usage, sleeping disturbance, autoimmune disease, psychopharmacologic medication use, and Type-A behavior were possible risk factors relating to the occurrence of CSC.

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Central serous chorioretinopathy (CSC) is a kind of retinopathy for the characteristics of neuroepithelium detachment with subretinal fluid accumulating mainly at the posterior pole of the fundus. Although no extensive and detailed epidemiological data has been published yet, except for several population-based surveys, it has been widely considered as the fourth most common non-surgical retinal disease after age-related macular degeneration, diabetic retinopathy, and branch retinal vein occlusion. Patients with CSC may experience visual loss, distorted or blurred vision, and/or dark spot in the center of the vision field. Most of them recover spontaneously with a better visual acuity and improvement of the symptoms within 3 months; however, the recurrence rate is up to 50% without any treatments and 10% of patients with CSC have more than three recurrences when the follow-up lasts for 15 years, which demonstrate a poor prognosis such as retinal dysfunction and permanent visual loss.

Although the pathogenesis of CSC remains poorly understood and needs further basic research, several risk factors have been studied and some associations between them have been came into conclusion. Age, male sex, and smoking are relative definite factors...
reported by numerous single studies, pointing out that the number of male patients are nearly eight times that of female ones and mean ages of these studies fluctuate within 40 to 45 year old, although aged and children cases also existed. A number of other factors also draw the attention of investigators, including the race, treatment with corticosteroid, emotional stress, Type-A behavior, Helicobacter pylori (H. pylori) infection, sleep apnea, pregnancy, organ transplantation, autoimmune diseases, and etc. Since controversial results have been published in these studies because of a variety of limitations and different methods, doctors are facing difficulties in judging the reasons and giving some interventions for patients. Except for some reviews, no quantitative conclusions have been reached yet covering the above risk factors.

Therefore, we conducted a systematic review and meta-analysis to summarize the data extracted from including studies. To the best of our knowledge, this is the first meta-analysis concentrating on risk factors for CSC and it might be useful for doctors to decide the treatments and provide precautions for patients with higher risks and frequent recurrences.

**Materials and Methods**

*Search Strategy and Study Selection*

An electronic comprehensive literature search using the PubMed, Embase, Cochrane Library, China National Knowledge Infrastructure (CNKI), and VIP databases has been conducted to confirm appropriate studies with the language restricted to English and Chinese and related references from these studies were also screened. The last search was on March 11, 2015. Following search terms were used: “Central serous chorioretinopathy” or “CSC” or “Central serous retinopathy” in combination with “risk factors”.

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**Fig. 1.** Flow chart of study selection. OR, odds ratio; RR, rate ratio.
### Table 1. The Baseline Characteristics and Quality Assessments of Included Studies

<table>
<thead>
<tr>
<th>Included study</th>
<th>Country</th>
<th>Main ethnicity</th>
<th>Study design, LOE</th>
<th>Sample (n)</th>
<th>Mean/median age (years)</th>
<th>Sex (male/female, n)</th>
<th>Risk factors</th>
<th>Quality score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mansuetta et al&lt;sup&gt;23&lt;/sup&gt;</td>
<td>United States</td>
<td>White</td>
<td>Retrospective case-control study, 2b</td>
<td>69/55</td>
<td>46/41</td>
<td>47/22</td>
<td>39/16</td>
<td>1, 2, 3, 6, 9, 10, 13, 14, 15, 20, 22, 23</td>
</tr>
<tr>
<td>Roshani et al&lt;sup&gt;16&lt;/sup&gt;</td>
<td>Iran</td>
<td>White</td>
<td>Prospective case-control study, 2a</td>
<td>35/138</td>
<td>34.14/34.01</td>
<td>32/3</td>
<td>128/10</td>
<td>5, 22, 23</td>
</tr>
<tr>
<td>Cotticelli et al, 2006</td>
<td>Italy</td>
<td>White</td>
<td>Retrospective case-control study, 2b</td>
<td>23/23</td>
<td>47/50</td>
<td>22/1</td>
<td>22/1</td>
<td>4, 5</td>
</tr>
<tr>
<td>Carvalho-Reccia et al, 2001</td>
<td>United States</td>
<td>Mixed</td>
<td>Prospective case-control study, 2a</td>
<td>50/50</td>
<td>55/53</td>
<td>36/14</td>
<td>36/14</td>
<td>6, 11</td>
</tr>
<tr>
<td>Karadimas and Bouzas&lt;sup&gt;24&lt;/sup&gt;</td>
<td>Greece</td>
<td>White</td>
<td>Prospective case-control study, 2a</td>
<td>38/38</td>
<td>44.7/44.5</td>
<td>28/10</td>
<td>28/10</td>
<td>6, 10</td>
</tr>
<tr>
<td>Marta et al&lt;sup&gt;25&lt;/sup&gt;</td>
<td>Poland</td>
<td>White</td>
<td>Prospective case-control study, 2a</td>
<td>55/55</td>
<td>49.2/46.7</td>
<td>36/19</td>
<td>33/22</td>
<td>5</td>
</tr>
<tr>
<td>Chen et al&lt;sup&gt;26&lt;/sup&gt;</td>
<td>Chinese Taipei</td>
<td>Asian</td>
<td>Retrospective cohort study, 3</td>
<td>835/4175</td>
<td>41.64/41.63</td>
<td>616/219</td>
<td>1095/3080</td>
<td>1, 2, 4, 6, 7, 12</td>
</tr>
<tr>
<td>Brodie et al&lt;sup&gt;17&lt;/sup&gt;</td>
<td>United States</td>
<td>Mixed</td>
<td>Retrospective case-control study, 2b</td>
<td>48/48</td>
<td>55/54</td>
<td>38/10</td>
<td>38/10</td>
<td>2, 8</td>
</tr>
<tr>
<td>Haimovici et al, 2004</td>
<td>United States</td>
<td>Mixed</td>
<td>Retrospective case-control study, 2b</td>
<td>312/312</td>
<td>45.02/45.34</td>
<td>230/82</td>
<td>230/82</td>
<td>2, 6, 10, 15, 16, 17, 19, 20, 21</td>
</tr>
<tr>
<td>Tsai et al&lt;sup&gt;19&lt;/sup&gt;</td>
<td>Chinese Taipei</td>
<td>Asian</td>
<td>Retrospective cohort study, 3</td>
<td>320/1554</td>
<td>41.3/41.0</td>
<td>197/123</td>
<td>950/604</td>
<td>2, 3, 8, 9, 12</td>
</tr>
<tr>
<td>Eom et al, 2012</td>
<td>Korea</td>
<td>Asian</td>
<td>Retrospective case-control study, 2b</td>
<td>113/339</td>
<td>45.6/45.3</td>
<td>90/23</td>
<td>270/69</td>
<td>2, 8</td>
</tr>
<tr>
<td>Tittl et al&lt;sup&gt;18&lt;/sup&gt;</td>
<td>United States</td>
<td>Mixed</td>
<td>Retrospective case-control study, 2b</td>
<td>230/230</td>
<td>51.1/50.8</td>
<td>168/62</td>
<td>168/62</td>
<td>1, 2, 6, 13</td>
</tr>
<tr>
<td>Zhou et al&lt;sup&gt;27&lt;/sup&gt;</td>
<td>China</td>
<td>Asian</td>
<td>Retrospective case-control study, 2b</td>
<td>110/110</td>
<td>49.7/45.08</td>
<td>81/29</td>
<td>81/29</td>
<td>1, 2, 6, 13</td>
</tr>
<tr>
<td>Conrad et al, 2007</td>
<td>Germany</td>
<td>White</td>
<td>Prospective case-control study, 2a</td>
<td>31/31</td>
<td>44.8/44.6</td>
<td>25/6</td>
<td>25/6</td>
<td>18</td>
</tr>
<tr>
<td>Sun et al&lt;sup&gt;28&lt;/sup&gt;</td>
<td>China</td>
<td>Asian</td>
<td>Prospective case-control study, 2a</td>
<td>30/20</td>
<td>38.6/NA</td>
<td>26/4</td>
<td>17/3</td>
<td>23</td>
</tr>
<tr>
<td>Yannuzzi&lt;sup&gt;15&lt;/sup&gt;</td>
<td>United States</td>
<td>Mixed</td>
<td>Prospective case-control study, 2a</td>
<td>110/110</td>
<td>42.3</td>
<td>89/21</td>
<td>89/21</td>
<td>16</td>
</tr>
<tr>
<td>Xu et al&lt;sup&gt;29&lt;/sup&gt;</td>
<td>China</td>
<td>Asian</td>
<td>Prospective case-control study, 2a</td>
<td>72/70</td>
<td>NA</td>
<td>NA</td>
<td>16</td>
<td>16</td>
</tr>
</tbody>
</table>


LOE, level of evidence.
The inclusion criteria were listed as below: (1) concerning risk factors related to CSC; (2) risk factors must exist before the diagnosis of CSC; (3) comparative studies containing randomized controlled trial (RCT), retrospective or perspective case–control or cohort studies; (4) odds ratio (OR) or rate ratio values of each risk factors were reported with 95% confidence interval (CI) or raw data were given for calculating. Animal studies, case reports, abstracts, conference proceedings, repeated publications, unpublished materials, reviews, and editorials were excluded from our study.

Data Extraction and Study Quality Assessment

Data were screened closely and extracted independently by two investigators (B.L. and T.D.). A third reviewer (J.Z.) made the final decision when inconsistency occurred between the above two reviewers. Data were collected from the including studies as follows: first author, year of publication, country of study, ethnicity, study design, sample size, patients’ baseline data, number of patients with each risk factors, and OR with 95% CIs and variables of adjustment in both CSC and non-CSC groups.

The level of evidence of each study was evaluated using the GRADE system and the Newcastle-Ottawa Scale was applied for the quality of nonrandomized controlled studies. Study scored 7 or more stars was regarded as high quality.

Statistics Analysis

Unadjusted ORs were selected for being synthesized to indentify the degree of relationship between these risk factors and CSC happening. The heterogeneity test was conducted through the \( \chi^2 \) test on the basis of Cochrane Q and \( P \) statistic. No significant heterogeneity existed when the \( P \)-value was greater than 0.10 and \( I^2 < 50\% \) in heterogeneity test and the fixed-effect model was to be applied. On the contrary, a random-effect model was used. Publication bias was assessed by inverted funnel plot visual inspection for comparisons. Data analyses were performed by the software RevMan (version 5.3; Cochrane Collaboration, Oxford, United Kingdom). We considered results in our meta-analysis to be significant if a two-sided \( P \)-value was less than 0.05.

Results

Studies Characteristics

A total of 9839 eyes from 9839 patients in a total of 17 studies were included in this systematic review and meta-analysis (Figure 1), characteristics of which are listed in Table 1. The published time of these studies was from June 1986 to February 2015. Among 17 studies, 8 were prospective case–control studies, 7 were retrospective studies, and 2 were retrospective cohort studies. Countries in which studies had been conducted were given in detail: six in USA, three in China, two in Chinese Taipei, one each in Italy, Greece, Poland, Germany, Iran, and Korea. In total, the main ethnicity of six studies was the white, six was Asian, and the other five was mixed ethnicities. A total of 2481 patients were diagnosed with CSC and 1761 were male, whereas 7358 occupied the control group and 3249 of whom were male patients (sex information was not given in one study).

Gender

A total of 16 studies provided detailed gender statistics except one, whereas most of them had matched the gender during the study design. Eventually, three studies evaluated the association between male sex and CSC. No heterogeneity was found in these three ones (\( I^2 = 0\% \), \( P = 0.95 \) and fixed-effect model was applied subsequently, indicating no sex differences in CSC and control groups (OR = 0.95; 95% CI: 0.49–1.68, \( P = 0.75 \)) (Figure 2). No publication bias was found through the inverted funnel plot.

Coronary Heart Disease

The relationship of coronary heart disease and CSC was researched in three studies. We found no
significant differences between case and control groups (OR = 0.95; 95% CI: 0.94–1.82, \( P = 0.11 \)) with no heterogeneity (\( I^2 = 0\% \), \( P = 0.62 \)) (Figure 3). We did not detect publication bias after conducting the inverted funnel plot.

**Hypertension**

A total of eight studies reported hypertension having occurred before the diagnosis of CSC, the heterogeneity of which was moderate (\( I^2 = 57\% \), \( P = 0.02 \)). We concluded significant differences between CSC and control groups (OR = 1.7; 95% CI: 1.28–2.25, \( P = 0.0002 \)) (Figure 4). Subgroup analysis was conducted in whites, Asians, and United States (mixed ethnicities). One whites’ study concentrated on hypertension and the heterogeneity could not be reached with no significant differences in both groups (OR = 1.67; 95% CI: 0.68–4.11, \( P = 0.26 \)). Asians existed in four studies showing that hypertension was a significant risk factor for CSC (OR = 1.58; 95% CI: 1.11–2.24, \( P = 0 \) 01). The remaining three studies were from United States, in which the population component was not given in detail, and significant differences were found between two groups (OR = 1.70; 95% CI: 1.28–2.25, \( P = 0.0002 \)). No publication bias existed in the inverted funnel plot.

**H. Pylori Infection**

*H. pylori* infection before occurrence of CSC was described in three studies and no significant
heterogeneity was concluded ($I^2 = 26\%$, $P = 0.26$). After combination of data from these studies, *H. pylori* infection was evaluated to be a significant risk factor for CSC (OR = 3.12; 95% CI: 1.81–5.40, $P < 0.0001$) (Figure 5). The inverted funnel plot did not show any publication bias.

**Steroid Usage**

A total of seven studies concentrated on steroid usage before patients were diagnosed with CSC. In total, a relative high heterogeneity was reached ($I^2 = 84\%$, $P < 0.00001$) with significant difference between two groups (OR = 4.29; 95% CI: 2.01–9.15, $P = 0.0002$) (Figure 6). Subgroup analysis was performed according to ethnicities suggesting steroid usage being a significant risk factor among whites in two studies (OR = 8.22; 95% CI: 3.28–20.59, $P < 0.00001$); two studies of Asians showed that the use of steroid tended not to be a significant risk factor for CSC (OR = 1.79; 95% CI: 0.82–3.92, $P = 0.14$); and the other two United States studies found significant differences between two groups (OR = 5.64; 95% CI: 2.86–11.10, $P < 0.00001$).

Different method of steroid usage was summarized in four studies and their characteristics were listed in Table 2. Four studies referred inhalant/nasal steroids, four for oral methods, four for injective methods, two for dermatological steroids, and one for other usages. Above all, inhalant/nasal, oral, and injective methods of steroid seemed to be significant risk factors.

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**Fig. 5.** Unadjusted OR and 95% CIs of *H. pylori* infection for CSC.

**Fig. 6.** Unadjusted OR and 95% CIs of steroid usage for CSC.
Publication bias was not indicated by inverted funnel plot in the meta-analysis of this risk factor.

**Sleeping Disturbances**

Three studies regarded sleeping disturbances as a potential risk factor. No significant heterogeneity existed ($I^2 = 0\%$, $P = 0.95$), and the result indicated the significant difference in case and control groups (OR = 1.90; 95% CI: 1.28–1.83, $P = 0.002$) (Figure 7). No publication bias was discovered through inverted funnel plot as to these three studies on sleeping disturbances.

**Autoimmune Disease**

A history of autoimmune disease was collected in three studies, the heterogeneity of which was not significant ($I^2 = 0\%$, $P = 0.57$). Our meta-analysis found autoimmune disease to be a significant risk factor for CSC (OR = 3.44; 95% CI: 1.90–6.26, $P < 0.002$) (Figure 8). No publication bias was discovered through inverted funnel plot as to these three studies on autoimmune disease.

**Psychopharmacologic Medication Use**

Three studies investigated the previous psychopharmacologic medication use with no low heterogeneity ($I^2 = 0\%$, $P = 0.63$). Significant differences occurred between two group of patients (OR = 2.69; 95% CI: 1.63–4.45, $P = 0.0001$) (Figure 9). No publication bias was discovered through inverted funnel plot in this part of meta-analysis.

**Type-A Behavior**

Type-A behavior was considered to be related to CSC in three studies. Apparent heterogeneity was seen ($I^2 = 65\%$, $P = 0.06$), and after the application of random-effect model, significant differences were concluded between CSC and control groups (OR = 2.53; 95% CI: 1.08–5.96, $P = 0.03$) (Figure 10). No publication bias existed by applying inverted funnel plot on the above studies.

**Other Factors**

Some factors which were researched in less than three studies were concluded in Table 3, including their pooled effects. Among the 14 factors extracted, gastroesophageal reflux disease, peptic ulcer, antihistamines usage, antacids/antireflux agents, psychological stress, pregnancy, and alcohol use could be regarded as significant risk factors, although urbanization level might be a protective factor for CSC. Nevertheless, valid relationship between these factors and CSC could not be confirmed because of lack of quantity of quality of concerning studies.

**Discussion**

This systematic review and meta-analysis consisted 9839 patients from 17 studies and to the best of our knowledge, it is the first meta-analysis concerning risk factors of CSC in detail. Statistics of 23 risk factors altogether were extracted and evaluated in our article, 9 of which were combined for further quantitative analyses because of having been referred in more than...
Our meta-analysis indicated that hypertension, *H. pylori* infection, steroid usage, sleeping disturbance, autoimmune disease, psychopharmacologic medication use, gastroesophageal reflux disease, peptic ulcer, antihistamines usage, antacids/antireflux agents, psychological stress, pregnancy, and alcohol use were significant risk factors relating to the occurrence of CSC, although urbanization level might be a potential protective factor for CSC. However, some of them needed further systematic designed studies to confirm.

Central serous chorioretinopathy was used to be considered as one kind of vasospastic diseases until the occurrence of fundus fluorescein angiography, showing the primary lesions originated from retinal pigment epithelium. However, not until the indocyanine green angiography came out did most investigators support the hypothesis that choroidal vascular hyperpermeability played a main role in the pathogenesis of CSC. The pathogenesis of CSC related to corticosteroid still remains ambiguous, but a few studies reported corticosteroid could impact the choroidal circulation by increasing the vascular hyperpermeability or interfering some cytokines for autoregulation of blood vessels, the formation of Bruch membrane and the function of blood-retina barrier of retinal pigment epithelium. It worked synergistically with the sympathetic system and inhibited the parasympathetic system, which regulating the choroidal circulation directly.

Both the increase of exogenous and endogenous glucocorticoid could lead to CSC. A variety of studies demonstrated the significant relationship between steroid usage and CSC. Our meta-analysis further confirmed this result and found that not only the systematic use of steroid but also other methods such as inhalant or nasal steroids could cause CSC, which was in accordance with others’ studies. Endogenous hypercortisolism was also reported by Carvalho-Recchia et al and Bouzas et al to be a potential risk factor for CSC. Our study found that it was not a significant risk factor, nevertheless, only one included study concentrated on it and other existing case reports or case series might lack the strength of evidence because of no control groups.

People with Type-A behavior are more competitive, aggressive, and hostile and have the tendency to experience stress, sleeping disturbances, or other physical and emotional disorders. When patients are under psychological stress, neuroendocrine system is involved and triggers the sympathetic system and hypothalamic-pituitary-adrenal axis. Subsequently, catecholamine and corticosteroid are released and share the similar mechanism causing CSC as above.

Type-A behavior and stress could be related to a series of psychosomatic diseases leading CSC, such as gastroesophageal reflux reported by Mansuetta et al, peptic ulcer researched by Cotticelli et al, and sleeping disturbances referred by Eom et al. These were considered significant risk factors of CSC through our meta-analysis, which was similar to their studies. Correspondingly, antacids or antireflux agents and psychopharmacologic medication were applied on those patients and might not be independent risk factors, needing further studies for adjusted results. Eom et al found that medical plant relieving emotional stress rather than psychopharmacologic drugs was a significant risk factor owing to Korean’s accustoms.

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**Fig. 8.** Unadjusted OR and 95% CIs of autoimmune disease for CSC.

**Fig. 9.** Unadjusted OR and 95% CIs of psychopharmacologic medication use for CSC.
In addition, our meta-analysis indicated pregnancy was a significant risk factor for CSC explained by excess amount of catecholamine and corticosteroid in their blood. Nevertheless, limited studies included supported this point of view and more detailed comparative studies are needed for intensive conclusions.

Patients bearing autoimmune diseases or organ transplantation usually had the history of corticosteroid treatments. Both factors were believed to be significant for CSC happening in our meta-analysis. Haimovici et al’s study indicated that autoimmune disease was still a significant risk factor after adjusted for corticosteroid. The possible pathogenesis might be connected with abnormal immune materials deposing on retinal pigment epithelium and choriodal layers, remaining controversial and lacking basic experiments. Since hardly any patients with autoimmune diseases received no treatments, this opinion requires greater strict studies and has difficulty being confirmed.

Persistent or untreated hypertension affects arterioles systematically including choriodal vessels by inducing repeated vasoconstriction, followed by occlusion of choriocapillaris and disrupt of the blood-retina barrier. Furthermore, people with Type-A behavior are more likely to develop hypertension than others, contributing to CSC together.

We analyzed hypertension could be a risk factors for CSC significantly after combination of eight studies, but conflict existed among several studies. Tittl et al and Haimovici et al drew the same conclusion with us, whereas Chen et al study opposed this opinion. Since hypertension was usually researched in retrospective studies, some bias such as uncontrolled factors and mistaken recalls.

_{H. pylori} infection has been considered to result atherosclerosis increasingly through its cytotoxin causing cascade damage of vessel walls. Dysfunction of choroidal microcirculation and endothelia cells leads to CSC. Three studies speculated _H. pylori_ infection was associated with CSC significantly, the combination of which reached the similar result by our meta-analysis. However, a portion of patients infected with _H. pylori_ could not be detected with existing laboratory examination, causing bias to original studies and our meta-analysis.

Although several positive results came out in our meta-analysis, some limitations exist and affect the validity of our study. First, most risk factors appeared in insufficient literature (less than five) and the

### Table 3. Other Risk Factors Relating to the Occurrence of CSC

<table>
<thead>
<tr>
<th>Potential risk factors</th>
<th>Number of studies</th>
<th>Heterogeneity</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastroesophageal reflux disease</td>
<td>2</td>
<td>65%</td>
<td>3.29 (1.04–10.34)</td>
</tr>
<tr>
<td>Peptic ulcer</td>
<td>2</td>
<td>0%</td>
<td>1.56 (1.30–1.88)</td>
</tr>
<tr>
<td>Organic transplantation</td>
<td>2</td>
<td>0%</td>
<td>6.30 (0.85–46.94)</td>
</tr>
<tr>
<td>Urbanization level</td>
<td>2</td>
<td>0%</td>
<td>0.86 (0.76–0.98)</td>
</tr>
<tr>
<td>Antihistamines</td>
<td>2</td>
<td>36%</td>
<td>2.93 (1.62–5.31)</td>
</tr>
<tr>
<td>Tobacco use</td>
<td>2</td>
<td>0%</td>
<td>1.16 (0.81–1.67)</td>
</tr>
<tr>
<td>NSAIDs usage</td>
<td>1</td>
<td>NA</td>
<td>0.97 (0.84–1.13)</td>
</tr>
<tr>
<td>Endogenous Cushing syndrome</td>
<td>1</td>
<td>NA</td>
<td>5.21 (0.24–111.24)</td>
</tr>
<tr>
<td>Antacids/antireflux agents</td>
<td>1</td>
<td>NA</td>
<td>15.00 (1.91–117.58)</td>
</tr>
<tr>
<td>Psychological stress</td>
<td>1</td>
<td>NA</td>
<td>59.35 (8.14–432.57)</td>
</tr>
<tr>
<td>Critical life-events</td>
<td>1</td>
<td>NA</td>
<td>9.49 (2.18–41.28)</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>1</td>
<td>NA</td>
<td>4.64 (1.88–11.43)</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>1</td>
<td>NA</td>
<td></td>
</tr>
</tbody>
</table>

The bold numbers mean \( P < 0.05 \).

NSAID, nonsteroid antiinflammatory drug.
combining data were not convincible enough. Second, no RCT trials were searched because studies on risk factors were partially restricted by ethics. Almost half of included studies were retrospective, bringing about bias which could not be interfered or changed. Third, the literature was mainly based on whites and Asians, other ethnicities such as Africans were not concerned, and some studies from United States did not describe the population in detail. The overall results might not be applicable to a variety of ethnicities. Finally, the time span of the literature was from 1986 to 2015, therefore, risk factors changed with environment and lifestyle, distributing inconsistently in different period. Above limitations may probably affect the strength of associations found in our study.

Conclusion

Our systematic review and meta-analysis concluded that hypertension, *H. pylori* infection, steroid usage, sleeping disturbance, autoimmune disease, psychopharmacologic medication use, Type-A behavior, gastrointestinal reflux disease, peptic ulcer, antihistamines, antacids/anti reflux agents, psychological stress, pregnancy, and alcohol use might be significant risk factors relating to the occurrence of CSC, although urbanization might be a potential protective factor. In consequence, judgments of reasons of CSC and follow-up treatments might be oriented to these factors. Undoubtedly, further prospective studies with larger samples and precise controls are demanded for more accurate and reliable conclusions.

Key words: central serous chorioretinopathy, meta-analysis, risk factors, systematic review.

References