

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Clinico-epidemiology and aetiopathogenesis of gallstone disease in the South Asian region: a scoping review protocol
AUTHORS	Weerakoon, Harshi; Vithanage, Ishari; Alahakoon, Oshadhi; Weerakoon, Kosala

VERSION 1 – REVIEW

REVIEWER	Nagem, Rachid Federal University of Minas Gerais
REVIEW RETURNED	13-Nov-2021

GENERAL COMMENTS	I believe “native Indians” (line 16) prefer to be called “native Americans”
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REVIEWER	Jørgensen, Torben Frederiksberg Hospital
REVIEW RETURNED	14-Dec-2021

GENERAL COMMENTS	This is a standard protocol describing how to perform a literature review. When the review is done a manuscript should be forwarded. I see no reason to publish a protocol, which just follows the textbooks.
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REVIEWER	Mendez-Sanchez, Nahum Medica Sur Clinic and Foundation, Liver Research Unit
REVIEW RETURNED	25-Feb-2022

GENERAL COMMENTS	<p>Manuscript Title: Clinico-epidemiology and aetiopathogenesis of gallstone disease in the South Asian region: a scoping review protocol Manuscript ID: bmjopen-2021-057808 This is an interesting protocol about epidemiology and aetiopathogenesis of gallstones disease in South Asian region. I have some comments.</p> <p>Page 3. Introduction section. What about the infectious as a risk factor for gallstone disease as well as the genetics? I suggest to include that information.</p> <p>Page 3. Introduction section. I suggest to describe in a short paragraph the demographic and ethnical characteristics of the South Asian region.</p> <p>Pages 3-4. I suggest to use reference 1 for pathophysiology section.</p> <p>Stage 3: Selection of eligible studies.</p> <ul style="list-style-type: none">• What about the genetics studies?
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	<ul style="list-style-type: none"> • Specify why do you include studies only from this period January 2000 to September 2021? • Why do you include only studies published in English language? I suggest to include other languages. Because you could miss a lot of information <p>Page 9. References section. The reference 1 and 16 is the same.</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1 (Dr. Rachid Nagem, Federal University of Minas Gerais)

Comment: I believe “native Indians” (line 16) prefer to be called “native Americans”

Response: Revised as suggested

Reviewer: 3 (Prof. Nahum Mendez-Sanchez, Medica Sur Clinic and Foundation)

Comment: Page 3. Introduction section. What about the infectious as a risk factor for gallstone disease as well as the genetics? I suggest to include that information.

Response: This information is now included as follows,

Pathogenesis of pigment stones are different from that of cholesterol stone. Black pigment stones mainly consisting of calcium bilirubinate is commonly associated with chronic haemolytic diseases. On the other hand, brown pigment stones; the GS rich in calcium palmitate are known to occur following biliary tract obstruction. [1,12] However, recent metagenomic studies have identified bacterial colonies even from cholesterol GS, indicating a possible role of gut bacteria in pathogenesis of cholesterol GS. [13]

Comment: Page 3. Introduction section. I suggest to describe in a short paragraph the demographic and ethnical characteristics of the South Asian region.

Response: A new paragraph on South Asian region is included as follows,

Afghanistan, Bangladesh, Bhutan, India, Maldives, Nepal, Pakistan, and Sri Lanka the countries situated in the southern part of the Asian continent facing the Indian ocean is collectively known as South Asia. [24] South Asian region was the home for ‘Indus civilization’ one of the well-known ancient civilizations. South Asia is the habitat for ~1.9 billion people, nearly one quarter of the world’s population. However, it is the 2nd least developed region in the world after the Sub-Saharan area. According to the world bank classification, the countries in South Asian region are classified as lower middle income countries except Afghanistan which is classified as a low income country. [24] It is a region with a high genetic diversity probably due to mixing of different groups of people since the ancient times due to its geo-climatic characteristics. [25,26] Ethnic and religious diversity is also high among South Asians. For example, over 4,000 well-defined communities live in India [27]. Though all these factors together could cause a huge complexity in peoples’ living, it is a region united by a common cultural and lifestyle habits. This can be mainly due to their religious background and the availability of limited resources due to the poor economic status.

Comment: Pages 3-4. I suggest to use reference 1 for pathophysiology section.

Response: Included.

Comment: Stage 3: Selection of eligible studies. What about the genetics studies?

Response: This is now included

Comment: Specify why do you include studies only from this period January 2000 to September 2021?

Response: This scoping review aims to discuss the current pattern of clinico-epidemiology and aetiopathogenesis of gallstone disease in the South Asian region as it is the key to identify possible control and preventive strategies of gallstone disease among South Asians. Thus, we decided to explore the nature of the disease over the last two decades as it will provide us a comprehensive picture of the current disease status and recent trends. This information is now included in the revised manuscript.

Studies published since January 2000 to April 2022 will be included as this scoping review aims to identify the current status of the disease in South Asia

Comment: Why do you include only studies published in English language? I suggest to include other languages. Because you could miss a lot of information.

Response: Thank you very much for pointing this out. However, South Asia is one of the most linguistically diverse areas in the world. According to the current literature South Asians are using ~650 languages and thus practically it will not be possible to translate all the languages correctly. As this might introduce significant amount of false information, Hence, authors decided to include only studies published in English. Most of the South Asian countries use English in scientific communications and most of the journals available at present are in English. Hence, we believe that we can review a substantial amount of information on GS disease by including studies published in English. Further, we have considered this as one limitations of this study under the strengths and limitations section.

'Only studies published in English will be included in the review'.

Comment: Page 9. References section. The reference 1 and 16 is the same.

Response: Corrected

VERSION 2 – REVIEW

REVIEWER	Mendez-Sanchez, Nahum Medica Sur Clinic and Foundation, Liver Research Unit
REVIEW RETURNED	30-Mar-2022
GENERAL COMMENTS	I have no comments at this time