Author’s response to reviews

Title: Moyamoya Disease: A Clinical Spectrum Literature Review and Case series from a Tertiary care hospital in Pakistan.

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Author’s response to reviews: see over
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Title: Moyamoya Disease: A Clinical Spectrum Literature Review and Case series from a Tertiary care hospital in Pakistan.

Version: 1
Date:

Dear Editors,
Please find our responses to the two reviews below. We have revised the manuscript according to the comments. The manuscript has also been conformed according to the journal style.

We hope this manuscript is now acceptable for your journal. Please let us know if you need any further revisions.

Regards,

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Reviewer: Peter Berlit

Thank you for your comments on our paper. We have addressed all your comments and revised the manuscript accordingly. Please find below our responses to your comments:

Major compulsory revisions

Comment 1: In some cases potential differential diagnoses like postpartum vasopathy and inflammatory angiopathy should be discussed in more detail.

Response: Discussion Para 14: Postpartum cerebral angiopathy and inflammatory angiopathy are two important differential diagnoses that may present with cerebral ischemia and imaging consistent with intracranial vasculopathy mimicking moyamoya disease.[37, 38]

Comment 2: Which diagnostic procedures were used for the diagnosis (angiography or MRA?).

Response: Methods Para 1: All patients received an MRI and MRA, and in those whose findings were suggestive but not clear or those that required further intervention received a 4 vessel cerebral angiogram.

Comment 3: It is unlikely that corticosteroids influence the outcome of the disease. What was the rationale to give steroids in the cases reported?

Response: We agree with the reviewer that steroids have no role in the management of stroke from moyamoya, this is a record of the individual practice of the treating physician in that case. We have modified our statement and made it a neutral statement.

Results Para 8: ’2 (15.4%) received steroids at the discretion of the treating physician’
Reviewer: Edward Smith

Thank you for your comments on our paper. We have addressed all your comments and revised the manuscript accordingly. Please find below our responses to your comments.

Comment 1: A lack of a consistent method of diagnosis of moyamoya. The diagnosis is made by angiogram, and – in some papers – with MRI/MRA. However, in this paper it is unclear, but appears that these authors have patients that were diagnosed without either of these modalities.

Response: Methods Para 1: All patients received an MRI and MRA, and in those whose findings were suggestive but not clear or those that required further intervention received a 4 vessel cerebral angiogram.

Comment 2: In addition, it is unclear that the authors make a distinction between moyamoya disease (the idiopathic presentation of bilateral angiographic moyamoya findings) and moyamoya syndrome (the presence of angiographic moyamoya in the setting of associated conditions, such as congenital cardiac disease, unilateral changes or other syndromic conditions).

Response: Background Para 1: Moyamoya disease is a rare progressive vaso-occlusive disorder of an unknown etiology. It is characterized by progressive stenosis of terminal portions of internal carotid arteries bilaterally, and the main trunks of Anterior and Middle Cerebral Artery, and is associated with collateral vessels at the base of the brain ('moyamoya' vessels).[1] When similar clinical manifestations are associated with an underlying disorder, it is referred to as Moyamoya syndrome. However, since the diagnostic criteria of this disease are mainly based on angiographic findings, it is recommended that the term Moyamoya 'syndrome' should be avoided at best.

Comment 3: The imaging provided is concerning (at least on the limited resolution images available) in at least in one case for the possibility of aneurysmal or dissection-related subarachnoid hemorrhage (Figure 1) – suggesting a need for more convincing images or questioning the diagnosis.

Response: Images are revised.

Comment 4: a much more robust method of confirming the diagnosis – using the accepted international diagnosis of moyamoya syndrome/disease – needs to be provided, with correlative images and - ideally – further data such as Suzuki grade.
Response: In this retrospective review, although this level of clarity would be ideal we were not able to report a Suzuki grade on all patients and therefore did not make it a part of the results.

Comment 5: If these follow-up data are not available, perhaps the focus of the paper should be on presentation and diagnosis – not speculative comments on management.

Response: The discussion has been shortened and focus shifted to presentation and diagnosis. A concerted effort has been made to remove all speculative statements and acknowledge the data limitations.

Comment 6: Although a rationale must have been present in each case, the reader is left without any information about why a particular strategy (surgical, medical, etc.) was selected for a given patient.

Response: It is difficult to comment on specific rationales for strategy in each case since the setting is a fee for service tertiary care centre. These decisions were made not purely on a scientific basis, individual affordability, practicing surgeons comfort level and expertise with procedure all played into the treatment decisions. In general, intervention for moyamoya is offered as the last resort and is often an indirect vascularization. Expertise for direct vascularization is not available in Pakistan – these procedures are performed with visiting neurosurgeons from other countries, if at all.

Comment 7: A more focused approach delineating the data collected and specifically discussing the limitations of treating and managing patients in Pakistan would be of greater value.

Response: Discussion last Para: Moyamoya disease, although a rare disorder in the Pakistani population, is perhaps going undiagnosed at large. Diagnosis requires expensive radiological studies and trained neurophysicians that are not available in most parts of the country. Additionally, the lack of neurosurgeons and their expertise in highly sophisticated procedures involved in the treatment makes it further difficult to manage a moyamoya patient.

Comment 8: The discussion should be significantly shortened and redirected to addressing the issues specific to Pakistani patients with moyamoya (difficulties with diagnosis, follow-up, differences in presentation, etc.)

Response: Please see Response to Comment 7.

Minor Revisions

1 – A need to provide percentages as well as absolute numbers.

Done
2- Providing a definition of moyamoya disease vs. syndrome.

Done

3 – A discussion of the CSF analysis.

Response: Results Para 5: Of the thirteen patients in this study, those that presented with fever and seizures (6; 46.2%) got a lumbar puncture. 4 (66.7%) had a normal CSF, 2 (33.3%) had a moderate rise in proteins showing a level of 70 mg/dl. None had a positive culture.

4 – Stylistic changes, such as grammatical review and perhaps changing the use of some less-commonly used words and phrases (“dumb” perhaps to “aphasic”) or removal of imprecise terms (“a good period”).

Done