Prevalence of Complications in Eyes With Nanophthalmos or Microphthalmos: A Systematic Review and Meta-analysis

Naseer Ally (naseerally@gmail.com)
University of the Witwatersrand https://orcid.org/0000-0002-6676-9352
Sarah Ismail
University of the Witwatersrand
Hassan Dawood Alli
University of the Witwatersrand

Protocol

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Abstract

Introduction

Microphthalmos and nanophthalmos are uncommon ocular conditions, whereby affected eyes have smaller dimensions compared to the normal population. Microphthalmos and nanophthalmos present several challenges to ophthalmologists; They have spontaneous and post-operative sequelae such as high hyperopia, angle-closure glaucoma, uveal effusion syndrome, and retinal detachment.

This systematic review and meta-analysis intends to assess the prevalence of both the spontaneous complications associated with nanophthalmos and microphthalmos, as well as the post-surgical complications associated with nanophthalmos or microphthalmos.

Methods and analysis

Articles will be searched for, on four online databases: PubMed, EMBASE, Scopus and Web of Science. Two independent reviewers will identify the studies according to prespecified inclusion and exclusion criteria. Relevant data will be extracted and assessed for the risk of bias in each article. The data will then be pooled to determine the prevalence of complications among patients with microphthalmos and nanophthalmos. If any preventative measures are associated with lower risks of developing complications, these will be expressed as odds ratios.

Discussion

Although nanophthalmos is an uncommon condition that affects the eye, its management and complications can be sight-threatening. Thus, it is important to counsel parents and patients correctly upon diagnosis and prior to any surgical intervention. This can only be done if the overall prevalence of complications is known.

Registration

This systematic review has been submitted to PROSPERO for registration.

Background

Microphthalmos and nanophthalmos are uncommon ocular conditions where the size of the eye is smaller than that of the normal population. [1–3] Axial length, the parameter most commonly used to measure the ocular size, is shorter in these eyes. Microphthalmos is divided into simple microphthalmos which has no associated ocular malformations, or complex microphthalmos, in which ocular malformations or systemic syndromes are present.[1,3] Nanophthalmos is a subset of simple microphthalmos where, in addition to the shorter axial length, the eye also has a thickened sclera and choroid.[2] This is thought to occur as a result of an abnormality in the arrangement of the collagen fibrils.[4] The terms microphthalmos and nanophthalmos are often used interchangeably and the absolute limit for the definition of shortened axial length varies, and is the subject of debate.[5] It is usually taken as an axial length of less than two standard deviations from the normal for age.[6] The absolute limit described in the literature are; <21.0mm[5,7], < 20.9mm[6], < 20.5mm[8,9], < 20mm[10], < 18.5mm[3], and < 17mm.[11] When there is a relative shortening of either the anterior or posterior segments of the eye, this is

known as relative anterior or posterior microphthalmos respectively.[1] Other parameters measured for microphthalmos and/or nanophthalmos include; shallow anterior chamber, high hyperopia, posterior wall thickness greater than 1.7mm and a high lens/eye volume ratio.[1,2]

Microphthalmos and nanophthalmos present several vision-related challenges to ophthalmologists which can occur spontaneously, or after surgery. Spontaneous vision-related problems are high hyperopia, angle-closure glaucoma, uveal effusion syndrome, and retinal detachment.[1,2] Other associations include corneal steepening, enlarged foveal avascular zone, optic disc drusen, central retinal vein occlusion, and chorioretinal folds.[1,2,11]

Surgery in nanophthalmos and microphthalmos is associated with higher rates of complications and poorer visual outcomes.[12] Cataract surgery is associated with complications such as anterior uveitis, uveal effusions, corneal decompensation, retinal detachment, cystoid macular oedema, choroidal haemorrhage, vitreous haemorrhage, and aqueous misdirection.[11,13] Management strategies to prevent these post-operative complications include the use of pre-operative steroids, pre-operative mannitol infusions, peripheral iridotomies and scleral lamellar resections.[9] Glaucoma surgery is also fraught with potential complications which include uveal effusion, choroidal folds, and cataract formation.

To date, reviews have been conducted which looked at the clinical spectrum and the treatment of complications in nanophthalmos. However, to our knowledge, there has been no systematic review looking at the prevalence of these complications among patients with microphthalmos or nanophthalmos. We, therefore, intend to undertake a systematic review and meta-analysis assessing the prevalence of both the spontaneous and post-surgical complications associated with nanophthalmos and microphthalmos.

Methods

Study design

This systematic review will include retrospective and prospective case series', cross-sectional studies, retrospective and prospective cohorts, and randomized clinical trials. It will be conducted according to the PRISMA-P (Preferred Reporting Items for Systematic Review and Meta-Analysis Protocol) guidelines.[14,15] This systematic review has also been submitted for registration on PROSPERO.[16]

Inclusion Criteria

The proposed inclusion criteria for this systematic review are as follows:

Population: All studies, with participants diagnosed with microphthalmos or nanophthalmos in one or both eyes, will be included if they have: i. more than 4 cases, and ii. defined microphthalmos/nanophthalmos as an axial length of < 21mm or a high lens/eye volume ratio. Nanophthalmos may have an additional diagnostic criterion of posterior wall thickness greater than 1.7mm.

Condition: The prevalence of the following complications will be assessed: High hyperopia (Spherical equivalent > 3D),[17] angle closure glaucoma, uveal effusion syndrome, retinal detachment, and chorioretinal folds.[1,2] Spontaneous ocular complications are defined as those ocular complications that are diagnosed prior

to any surgical procedure performed. If a surgical procedure occurred prior to the diagnosis, the study would fall under post-surgical complications.

Context: The studies will probably be hospital-based cohorts or case series. If population-based studies are found these will be included and analysed separately.

Since this is a prevalence study, no comparison group is necessary. However, there may be randomised studies using an intervention and comparing post-surgical complications. These complications will then be analysed according to the intervention and the comparison arms used. The comparison arm may an alternative intervention or placebo.

Exclusion criteria

Studies that will be excluded are: i. those that have not adequately defined the criteria for the diagnosis of nanophthalmos or microphthalmos, ii. studies that have less than five participants, iii. studies with criteria not defined above, and deemed unsuitable, and iv. studies in languages other than English with no published translation.

Databases and information sources

Four databases will be searched for relevant studies: PubMed, EMBASE, Web of Science and Scopus. Registered clinical trials that are published will also be sought on ClinicalTrials.gov. Reviews will be checked on the Cochrane database. The reference lists of these reviews and any reviews found on the other databases will be checked for additional articles. Where necessary, authors will be contacted for clarification by one reviewer (NA).

Search Strategy

The search strategy, using the search terms in Appendix A below, has been developed using the CoCoPop method above.[18] All the information and data will be collated and entered onto Microsoft Excel (Microsoft Corporation). The data collected will be assessed on the first 5 articles and amended if required.

Study selection

The study selection process will be conducted using the PRISMA guidelines and flow diagram.[14] After exclusion of duplicate studies using the Zotero™ citation manager, and after being rechecked manually, all titles and abstracts will be reviewed independently by two reviewers (NA and SI) according to the prespecified inclusion and exclusion criteria (Appendix B). Any disagreements will be resolved by a third reviewer (HDA). Systematic and narrative reviews, animal studies, editorials and letters will be excluded. The reference lists of review papers will be screened for studies that meet inclusion criteria. The full texts of eligible studies / papers will be examined for inclusion into the systematic review and meta-analysis (Appendix B). When data from the same cohort are reported in separate manuscripts, the study reporting the largest sample fulfilling our eligibility criteria will be selected. If there are doubts regarding these datasets, the corresponding authors will be contacted for clarification.

Studies that are included, and decisions made, will be recorded on Microsoft Excel™ (Microsoft Corporation).

Risk of bias assessment/Quality assessment

Studies assessing the prevalence of spontaneous complications and post-operative complications in cohorts and case series' will be assessed using a modified version of the Joanna Briggs Institute (JBI) critical appraisal tool.[18,19] If there are randomized clinical trials, they will be assessed for quality using the JBI assessment tool for randomised clinical trials[20] and the overall evidence will be assessed using the GRADE approach.[21]

Studies comparing the effect of surgical interventions on the prevalence of post-operative complications will be assessed for publication bias using a funnel plot.

Data extraction

Data will be extracted by one reviewer (NA), checked by another reviewer (SI), and populated onto Microsoft Excel™ (Microsoft Corporation). Disagreements will be resolved by a third reviewer (HDA). The following data will be extracted: Year of study, study design (i.e., Cohort, cross-sectional etc.), total number of participants, axial length, proportion of males to females, mean/median age at presentation, number of participants with one or more complications (High hyperopia [Spherical equivalent > 3D], angle closure glaucoma, uveal effusion syndrome, retinal detachment, and chorioretinal folds), posterior wall thickness and lens/eye volume ratio.

Data Analysis

Data will be analysed in Stata 16.1 (STATACorp LLC, College station, Texas). Due to the difference in definitions and diagnosis of microphthalmos and nanophthalmos a random effects models will be used throughout. The presence of spontaneous complications will be analysed using the "metaprop" command in Stata. The Freeman-Tukey double arcsine transformation will be performed to normalise outcomes before pooling the prevalence. Study specific 95% confidence intervals will be generated using the exact method. The I^2 statistic will be used to check for overall, intergroup, and intragroup heterogeneity. Forest plots will then be generated from the data.

For post-operative complications where a comparison group is used the effect size will be compared using the "meta esize" command. A random effects model will be used to present the overall effect size as an odd ratio with 95% confidence intervals. Forest plots will then be generated from the data. If possible, Egger's test and funnel plots will be used to test for publication bias.

Subgroups

Subgroups will be analysed according to axial length to see if the proportion of complications increases/decreases with decreasing axial length in both the spontaneous complication group and post-surgical complication group. Subgroups will also be analysed according to subtypes of microphthalmos (anterior, posterior, simple and complex) if the data permits this. If randomised trials are found using interventions to decrease the post-operative complications these will be meta-analysed using odds ratios to assess the odds of getting those complications post-operatively.

Discussion

Although microphthalmos and nanophthalmos are uncommon conditions that affect the eye, its management and complications can be sight-threatening.[1,2,8,12] Due to the conditions being uncommon, it is difficult to perform single-centre studies with large patient numbers. A systematic review and meta-analysis provides a valid method to assess the prevalence of complications in these patients. It is also important to counsel these patients correctly upon diagnosis and prior to any surgical intervention. Thus far, to our knowledge, there is no systematic review and meta-analysis assessing the prevalence of complications of patients with microphthalmos or nanophthalmos, that occur spontaneously, or after surgery. We believe that this will add valuable information to the body of knowledge on the subject.

Strengths And Weaknesses

This protocol is in line with the PRISMA guidelines for the conducting of systematic reviews and it has been registered on PROSPERO. Amendments to his protocol will be updated on the PROSPERO register.

Weaknesses include the inclusion of only English articles which means that articles in other languages may be missed, and possible heterogeneity in methodology (especially the definitions of microphthalmos/nanophthalmos) and data.

Abbreviations

PRISMA-P
Preferred Reporting Items for Systematic Review and Meta-Analysis Protocol

Declarations

Ethics approval and consent to participate: Not applicable

Consent for publication: Not applicable

Availability of data and material: Not applicable

Competing interests: None to declare

Funding: None to declare

Authors' contributions: NA, SI and HDA conceived, designed and wrote the protocol.

Authors’ information: Drs NA and HDA are consultant ophthalmologists at St John Eye Hospital. Dr NA is a consultant in the paediatric ophthalmology and vitreo-retinal clinic. Dr HDA works in the vitreo-retinal, uveitis and neuro-ophthalmology clinics. Dr SI is a fourth year registrar in ophthalmology.

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Supplementary Files

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- Appendix.pdf