Comment on "Infertility and teratogenicity after paternal exposure to systemic dermatologic medications: A systematic review"

To the Editor: We read with interest the article entitled "Infertility and teratogenicity after paternal exposure to systemic dermatologic medications: A systematic review" by Zakhem et al.[1] The considerations about dosage and duration of treatment related to the risk for infertility in male patients taking systemic dermatologic medications and evidence of potential teratogenicity in semen with the presence of medication are very relevant for clinical practice. However, we have some comments about this publication.

Systematic reviews are synthesis studies that must go through methodologic procedures to generate relevant information from primary studies in order to answer a predetermined research question. Therefore, authors must explicitly describe their methods in the manuscript. Systematic reviews provide the highest level of evidence for clinical practice in the evidence-based medicine framework, and they are important sources for the elaboration of clinical practice guidelines. Nevertheless, systematic reviews, given their inductive nature, might have problems that could negatively affect their validity and precision.[2] Specifically, in the Zakhem et al publication; the authors did not describe several elements that should have been reported in accordance to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement, the most important academic instrument that provides guidelines for the publication of systematic reviews.[3] Although there are several elements considered, we will focus on a crucial element: the absence of a report on the risk for bias assessment for the primary studies included.

In the clinical epidemiology arena, a crucial axiom is that the quality of primary studies used has a direct impact on the systematic review quality. The accuracy of the results of a study is structured in 2 parts: validity (internal and external) and precision. Specifically, internal validity is crucial, and it has 3 main threats: selection bias, information bias, and confounding.[4] Multiple tools have been developed to evaluate the risk for bias of primary studies included in systematic reviews. Enhancing the Quality and Transparency of Health Research network (http://www.equator-network.org) is an open-access source with different validated tools that can be consulted to assess the risk for bias and research quality. The review by Zakhem et al included randomized clinical trials and observational studies. In the case of clinical trials, the Cochrane Risk of Bias Tool is the most often used and suggested; this instrument can even be used alongside Review Manager software. On the other hand, for observational studies, the Newcastle-Ottawa scale and Scottish Intercollegiate Guidelines Network are the most recommended scales. The use of any of these would have improved the quality of the systematic review. Another important approach is Grading of Recommendations, Assessment, Development and Evaluations (GRADE).[5]

In addition, we deem that the results reported by this systematic review are important, but critical aspects of its quality must be evaluated. For this purpose, there are ad hoc instruments, such as Assessing the Methodological Quality of Systematic Reviews.[6] Its use will serve as a basis to perform an objective assessment of the evidence and have a critical stance for its subsequent application in clinical practice.

Gianfranco Enriquez-Gutierrez, BSc,[a] Fernando Sosaya-Muñoz, BSc,[a] Claudia Rojas-Varona, MD,[b,c] and Edward Mezones-Holguín, MD, MSc[c]

From the Faculty of Health Sciences, Universidad Peruana de Ciencias Aplicadas, Lima, Peru[a]; Department of Internal Medicine, Hospital Santa Rosa, Piura, Peru[b]; and Epi-gnosis Solutions, Piura, Peru[c]

Funding sources: None.

Conflicts of interest: None disclosed.

Correspondence to: Gianfranco Enriquez-Gutierrez, BSc, Universidad Peruana de Ciencias Aplicadas, Alameda San Marcos Cuadra 2, Lima, Chorrillos 15067, Peru

E-mail: fabrizioeg@hotmail.com

REFERENCES

1. Zakhem GA, Motosko CC, Mu EW, Ho RS. Infertility and teratogenicity after paternal exposure to systemic dermatologic medications: a systematic review. *J Am Acad Dermatol*. 2019;80(4):957-969.
2. Bolaños-Díaz R, Mezones-Holguín E, Gutiérrez-Aguado A, Málaga G. Los estudios de síntesis como base para las evaluaciones económicas en salud: necesidad de la valoración de su calidad. *Rev Peru Med Exp Salud Publica*. 2011;28(3):528-534.
3. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: the PRISMA statement. *PLoS Med*. 2009;6(7):e1000097.

4. Rothman K, Greenland S, Lash T. Design objectives of epidemiological studies. In: Rothman K, ed. *Modern Epidemiology*. 3rd ed. Lippincott Williams & Wilkins; 2012:96.
5. Guyatt GH, Oxman AD, Vist GE, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ (Clinical research ed.)*. 2008;336(7650): 924-926.
6. Pollock M, Fernandes RM, Hartling L. Evaluation of AMSTAR to assess the methodological quality of systematic reviews in overviews of reviews of healthcare interventions. *BMC Med Res Methodol*. 2017;17(1):48.

https://doi.org/10.1016/j.jaad.2018.12.065