Preeclampsia: Universal Screening or Universal Prevention for Low and Middle-Income Settings?

Daniel Lorber Rolnik[1] Mario Henrique Burlacchini de Carvalho[2] Guilherme Antonio Rago Lobo[3] Stefan Verlohren[4] Liona Poon[5] Ahmet Baschat[6] Jon Hyett[7] Basky Thilaganathan[8] Emmanuel Bujold[9] Fabricio da Silva Costa[10]

[1] Department of Obstetrics and Gynaecology, Monash University, Melbourne, Australia
[2] Department of Obstetrics and Gynecology, Universidade de São Paulo, São Paulo, SP, Brazil
[3] Department of Obstetrics, Escola Paulista de Medicina, Universidade Federal de São Paulo, São Paulo, SP, Brazil
[4] Department of Obstetrics, Charité Universitätsmedizin, Berlin, Germany
[5] Department of Obstetrics and Gynaecology, The Chinese University of Hong Kong, Hong Kong
[6] The Johns Hopkins Center for Fetal Therapy, Department of Gynecology and Obstetrics, The Johns Hopkins Hospital, Baltimore, United States
[7] RPA Women's and Babies, Royal Prince Alfred Hospital, Sydney, New South Wales, Australia
[8] Fetal Medicine Unit, St George's University Hospitals NHS Foundation Trust, London, United Kingdom
[9] Department of Obstetrics and Gynaecology, Laval University, Quebec, Canada
[10] Maternal Fetal Medicine Unit, Gold Coast University Hospital and School of Medicine, Griffith University, Gold Coast, Australia

Address for correspondence Daniel Lorber Rolnik, 27-31 Wright St, Clayton VIC 3168, Australia (e-mail: daniel.rolnik2@gmail.com).

Rev Bras Ginecol Obstet 2021;43(4):334–338.

Dear Editor,

We read with interest the Clinical Consensus Recommendation about screening and prevention of preeclampsia published by De Oliveira et al.[1] The authors recommend that identification of high-risk women should be based on maternal risk factors alone, and that universal treatment (of all pregnant women) with aspirin at a dose of 100 mg should be considered in low- and middle-income countries. In this letter, we express our concerns and disagreement with these strategies.

The association of certain maternal risk factors with an increased risk of preeclampsia development is well known, and several risk scoring systems have been recommended by Obstetric societies around the world, such as the National Institute for Health and Care Excellence (NICE) criteria in the United Kingdom, and the American College of Obstetrician and Gynecologists (ACOG) in the United States. Such scoring systems are based on experts' opinions and low levels of evidence, attribute similar weights to very different risk factors, and perform poorly in the clinical practice.[2] Recent large studies[2] have shown that such methods fail to identify as high-risk 60% to 70% of women who will later develop preeclampsia. Furthermore, physician compliance with these recommendations is low, with only 20% to 30% of high-risk women receiving aspirin prophylaxis.[2,3] On the other hand, combined screening with individual risk calculation by incorporating risk factors, mean arterial blood pressure, uterine artery Doppler studies, and placental growth factor (PlGF) far outperforms risk scoring, identifying as high-risk about three quarters of women who will develop preterm preeclampsia, and 90% of those destined to develop early-onset disease.[4,5] In addition, combined screening is more cost-effective,[6] and is associated with nearly total physician compliance.[3] Although resistance to new

DOI https://doi.org/10.1055/s-0041-1729953.
ISSN 0100-7203.

Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

technologies is common in Medicine, and translation of research into clinical practice usually takes a long time,[7] most components of combined screening, such as the measurement of arterial blood pressure and ultrasound are readily available and widely in use in most settings (even in low/middle-income countries). Simplified versions of the algorithm (for example, without biochemical markers) outperformed clinical history even in middle-income countries such as Brazil,[8,9] and could be rapidly implemented with minimal or no increase in cost, and lead to a significant increase in the detection of high-risk women who would benefit from aspirin prophylaxis and likely be missed by risk scoring screening.

As appealing as the suggestion to give aspirin to all pregnant women given its relative safety and low cost may be, a strategy of universal aspirin use has not been properly assessed in adequately-powered prospective studies.[10] Pregnant women are naturally resistant to medication use in the absence of convincing medical indication, and such an approach would likely be associated with low adherence to treatment.[10] The strong effect of aspirin in the prevention of preeclampsia in high-risk populations[11] may not be observed when the treatment is recommended to the entire obstetric population, and side effects will inevitably become more frequent if millions of women are treated. Indeed, data from a previous study on universal aspirin prophylaxis demonstrated no clear treatment benefit,[12,13] increased risk of postpartum hemorrhage,[14] and other hemorrhagic events,[12] as well as low adherence to treatment.[12] We argue that early combined prediction with the full or simplified versions of the algorithm for individual risk calculation is feasible in low- and middle-income countries, and should be the preferred method of screening whenever possible, in line with recent recommendations from the International Federation of Gynecology and Obstetrics (FIGO),[15] the International Society for the Study of Hypertension in Pregnancy (ISSHP),[16] and the International Society of Ultrasound in Obstetrics and Gynecology.[17]

Conflict of Interests

The authors have no conflict of interests to declare.

References

1 De Oliveira LG, Diniz ALD, Prado CAC, Da Cunha Filho EV, De Souza FLP, Korkes HA, et al. Pre-eclampsia: universal screening or universal prevention for low and middle-income settings? Rev Bras Ginecol Obstet. 2021;43(01):61–65. Doi: 10.1055/s-0040-1713803

2 Tan MY, Wright D, Syngelaki A, Akolekar R, Cicero S, Janga D, et al. Comparison of diagnostic accuracy of early screening for pre-eclampsia by NICE guidelines and a method combining maternal factors and biomarkers: results of SPREE. Ultrasound Obstet Gynecol. 2018;51(06):743–750. Doi: 10.1002/uog.19039

3 Guy GP, Leslie K, Diaz Gomez D, Forenc K, Buck E, Khalil A, Thilaganathan B. Implementation of routine first trimester combined screening for pre-eclampsia: a clinical effectiveness study. BJOG. 2021;128(02):149–156. Doi: 10.1111/1471-0528.16361

4 Rolnik DL, Wright D, Poon LCY, Syngelaki A, O'Gorman N, Matallana CP, et al. ASPRE trial: performance of screening for preterm pre-eclampsia. Ultrasound Obstet Gynecol. 2017;50(04): 492–495. Doi: 10.1002/uog.18816

5 O'Gorman N, Wright D, Poon LC, Rolnik DL, Syngelaki A, Wright A, et al. Accuracy of competing-risks model in screening for pre-eclampsia by maternal factors and biomarkers at 11-13 weeks' gestation. Ultrasound Obstet Gynecol. 2017;49(06):751–755. Doi: 10.1002/uog.17399

6 Park F, Deeming S, Bennett N, Hyett J. Cost effectiveness analysis of a model of first trimester prediction and prevention for preterm preeclampsia against usual care. Ultrasound Obstet Gynecol. 2020;•••;. Doi: 10.1002/uog.22193[ahead of print]

7 Papageorghiou AT. From evidence to implementation. BJOG. 2020;127(10):1173–1174. Doi: 10.1111/1471-0528.16408

8 Rocha RS, Alves JAG, E Holanda Moura SBM, Araujo EJúnior, Peixoto AB, Santana EFM, et al. Simple approach based on maternal characteristics and mean arterial pressure for the prediction of preeclampsia in the first trimester of pregnancy. J Perinat Med. 2017;45(07):843–849. Doi: 10.1515/jpm-2016-0418

9 Rocha RS, Gurgel Alves JA, E Holanda Moura SBM, Araujo EJúnior, Martins WP, Vasconcelos CTM, et al. Comparison of three algorithms for prediction preeclampsia in the first trimester of pregnancy. Pregnancy Hypertens. 2017;10:113–117. Doi: 10.1016/j.preghy.2017.07.146

10 Cuckle H. Strategies for prescribing aspirin to prevent preeclampsia: a cost-effectiveness analysis. Obstet Gynecol. 2020;135(01): 217. Doi: 10.1097/AOG.0000000000003631

11 Rolnik DL, Wright D, Poon LC, O'Gorman N, Syngelaki A, Matallana CP, et al. Aspirin versus placebo in pregnancies at high risk for preterm preeclampsia. N Engl J Med. 2017;377(07):613–622. Doi: 10.1056/NEJMoa1704559

12 Subtil D, Goeusse P, Puech F, Lequien P, Biausque S, Breart G, et al; Essai Régional Aspirine Mère-Enfant (ERASME) Collaborative Group. Aspirin (100 mg) used for prevention of pre-eclampsia in nulliparous women: the Essai Régional Aspirine Mère-Enfant study (Part 1). BJOG. 2003;110(05):475–484. Doi: 10.1046/j.1471-0528.2003.02096.x

13 Hoffman MK, Goudar SS, Kodkany BS, Metgud M, Somannavar M, Okitawutshu J, et al; ASPIRIN Study Group. Low-dose aspirin for the prevention of preterm delivery in nulliparous women with a singleton pregnancy (ASPIRIN): a randomised, double-blind, placebo-controlled trial. Lancet. 2020;395(10220):285–293. Doi: 10.1016/S0140-6736(19)32973-3

14 Mone F, Mulcahy C, McParland P, Breathnach F, Downey P, McCormack D, et al. *T*rial of feasibility and acceptability of routine low-dose aspirin versus *E*arly *S*creening *T*est indicated aspirin for pre-eclampsia prevention (*TEST* study): a multicentre randomised controlled trial. BMJ Open. 2018;8(07):e022056. Doi: 10.1136/bmjopen-2018-022056

15 Poon LC, Shennan A, Hyett JA, Kapur A, Hadar E, Divakar H, et al. The International Federation of Gynecology and Obstetrics (FIGO) initiative on pre-eclampsia: A pragmatic guide for first-trimester screening and prevention. Int J Gynaecol Obstet. 2019;145 (Suppl 1):1–33. Doi: 10.1002/ijgo.12802

16 Brown MA, Magee LA, Kenny LC, Karumanchi SA, McCarthy FP, Saito S, et al; International Society for the Study of Hypertension in Pregnancy (ISSHP) Hypertensive disorders of pregnancy: ISSHP classification, diagnosis, and management recommendations for international practice. Hypertension. 2018;72(01):24–43. Doi: 10.1161/HYPERTENSIONAHA.117.10803

17 Sotiriadis A, Hernandez-Andrade E, da Silva Costa F, Ghi T, Glanc P, Khalil A, et al; ISUOG CSC Pre-eclampsia Task Force. ISUOG Practice Guidelines: role of ultrasound in screening for and follow-up of pre-eclampsia. Ultrasound Obstet Gynecol. 2019; 53(01):7–22. Doi: 10.1002/uog.20105

