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Erkan Kalafat, MD, Amani Shirazi, Basky Thilaganathan, Professor, Asma Khalil, Professor

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The role of aspirin in prevention of preeclampsia in twin pregnancies: Does the dose matter?

Erkan KALAFAT, MD ^{1,2}

Amani SHIRAZI ¹

Basky THILAGANATHAN, Professor ^{1,3}

Asma KHALIL, Professor ^{1,3}

1. Fetal Medicine Unit, St George's Hospital, St George's University of London, UK.
Cranmer Terrace, London SW17 0RE

2. Department of Statistics, Faculty of Arts and Science, Middle East Technical
University

3 Vascular Biology Research Centre, Molecular and Clinical Sciences Research
Institute, St George's University of London, Cranmer Terrace, London SW17 0RE,
UK.

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CORRESPONDENCE

Professor Asma Khalil

Fetal Medicine Unit,

St George's University of London,

London SW17 0RE

Telephone: (Work) +442032998256,

Mobile: +447917400164.

Fax: +442077339534

E-mail: akhalil@sgul.ac.uk; asmakhalil79@googlemail.com

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Objective: The aspirin use in twin pregnancies for prevention of preeclampsia is a controversial topic and the evidence on the required dose of aspirin is scarce. We aimed to assess the efficacy of 75mg/day versus 150mg/day aspirin for prevention of preeclampsia in twin pregnancies.

Study Design: This is a retrospective cohort study of twin pregnancies managed at St. George's University Hospital between 2012 and 2019. The National Institute for Health and Care Excellence (NICE) guideline published in 2010 has recommended low-dose aspirin to women at high risk of preeclampsia.¹ Monochorionic and dichorionic twin pregnancies were included in the cohort. Pregnancies between 2010 and 2012 were excluded to ensure thorough implementation of national guideline. High-order multi-fetal gestations and pregnancies complicated by fetal anomalies were also excluded. Twin pregnancies with any of these risk factors (hypertension in a previous pregnancy, chronic hypertension, renal disease, autoimmune disorder, diabetes, nulliparity, maternal age >40 years, pregnancy interval >10years, body mass index >35kg/m² or family history of preeclampsia) as per NICE guideline were started on aspirin¹. The aspirin dose was changed from 75mg/day to 150mg/day after 2017, following reports of effective prevention of preeclampsia using aspirin 150mg/day.²⁻⁴ The main outcome was preeclampsia diagnosed according to International Society for the Study of Hypertension in Pregnancy guideline.⁵ Hypertensive disorders of pregnancy (HDP) included preeclampsia or gestational hypertension.

Results: There were 630 pregnancies in the cohort; 404 received aspirin (108 received 150mg/day and 296 received 75mg/day), while 226 did not. There were 28 (4.4%) cases of preeclampsia and 47 (7.5%) cases of HDP in the cohort. No significant differences in maternal age ($P=0.510$), nulliparity ($P = 0.945$), chorionicity ($P=0.700$) were observed between 75mg/day and 150mg/day aspirin groups.

The incidence of preeclampsia was similar between aspirin 150mg/day and no aspirin groups (1.8% vs. 3.1%, $P=0.510$). However, there was a trend towards a significant decrease in preeclampsia in those receiving aspirin 150mg/day compared to 75mg/day (1.8% vs 6.4%, $P=0.067$). There were no statistically significant differences between aspirin 150mg/day and no aspirin groups regarding the incidence of HDP (1.8% vs 5.3%, $P=0.140$), but the incidence of HDP was significantly lower in aspirin 150mg/day group compared to 75mg/day (1.8% vs 11.1%, $P =0.003$) (Figure 1). The incidence of HDP was significantly higher in aspirin 75mg/day group compared to no aspirin (11.1% vs 5.3%, $P=0.018$).

We investigated the association of aspirin dose with HDP in a multivariable logistic regression model after adjusting for maternal age in years, chorionicity, and smoking during pregnancy. The reference group was the low-risk twin pregnancies who did not receive aspirin. The direction of the association changed from a significant increase in HDP (odds ratio: 2.01, 95% confidence interval: 1.03-4.18, $P=0.048$) to a non-significant decrease (odds ratio: 0.31, 95% confidence interval: 0.05-1.16, $P =0.127$) when the aspirin dose was increased from 75mg/day to 150mg/day.

Conclusion: The incidence of hypertensive disorders in twin pregnancies with additional risk factors for preeclampsia was significantly lower in those receiving aspirin 150mg/day compared to 75mg/day.

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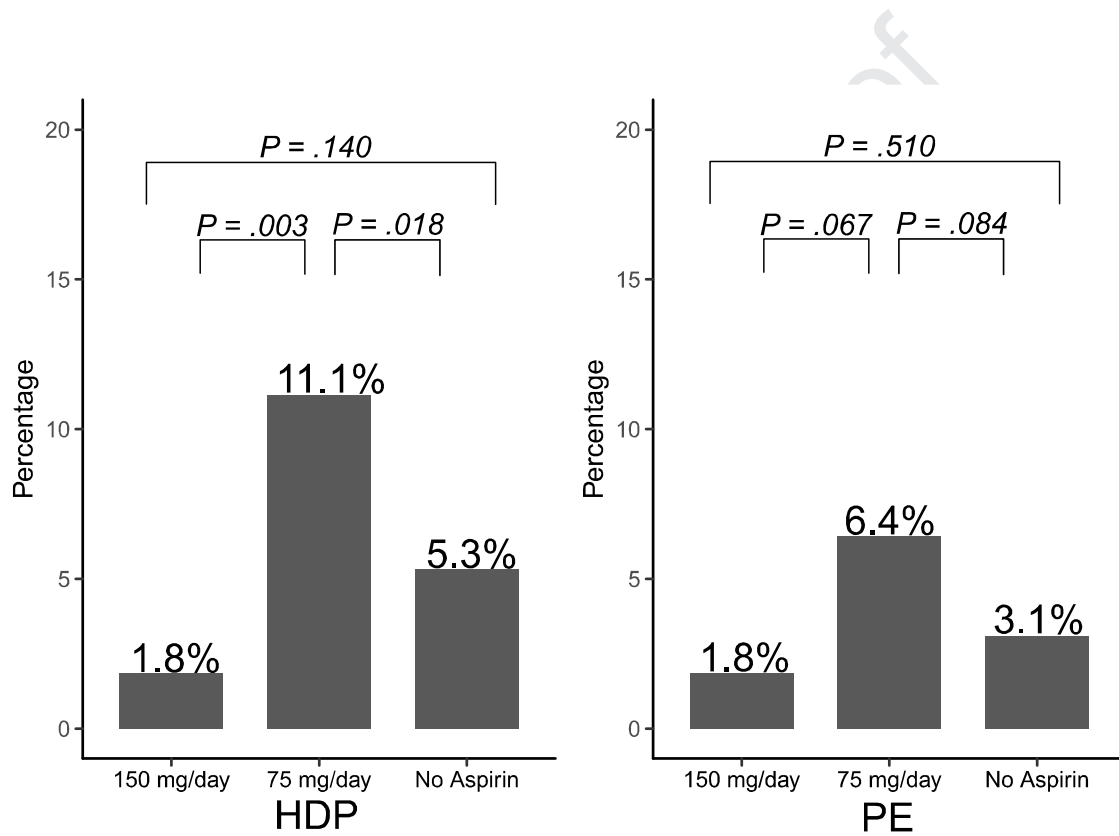
REFERENCES:

1. National Institute for Health and Care Excellence. Hypertension in pregnancy: diagnosis and management (NICE guideline [NG133]). 2019. Available at <https://www.nice.org.uk/guidance/ng133> [Accessed February 2020]
2. Rolnik DL, Wright D, Poon LC, O'Gorman N, Syngelaki A, de Paco Matallana C *et al.* Aspirin versus placebo in pregnancies at high risk for preterm preeclampsia. *N Engl J Med.* 2017;377:613-622. doi:10.1056/NEJMoa1704559
3. Poon LC, Wright D, Rolnik DL, Syngelaki A, Delgado JL, Tsokaki T *et al.* Aspirin for evidence-based preeclampsia prevention trial: Effect of aspirin in prevention of preterm preeclampsia in subgroups of women according to their characteristics and medical and obstetrical history. *Am J Obstet Gynecol.* 2017;217:585 e581-585 e585. doi:10.1016/j.ajog.2017.07.038
4. Roberge S, Nicolaides K, Demers S, Hyett J, Chaillet N, Bujold E. The role of aspirin dose on the prevention of preeclampsia and fetal growth restriction: Systematic review and meta-analysis. *Am J Obstet Gynecol.* 2017;216:110-120 e116. doi:10.1016/j.ajog.2016.09.076
5. Tranquilli AL, Dekker G, Magee L, Roberts J, Sibai BM, Steyn W *et al.* The classification, diagnosis and management of the hypertensive disorders of pregnancy: A revised statement from the issHP. *Pregnancy Hypertens.* 2014;4:97-104. doi:10.1016/j.preghy.2014.02.001

Figure 1. The incidence of preeclampsia (right) and hypertensive disorders of pregnancy (preeclampsia or gestational hypertension) (left) in women with twin pregnancies who received 150mg/day vs 75mg/day and no aspirin.

The *P* values were calculated with chi-squared test.

PE: preeclampsia, HDP: hypertensive disorders of pregnancy



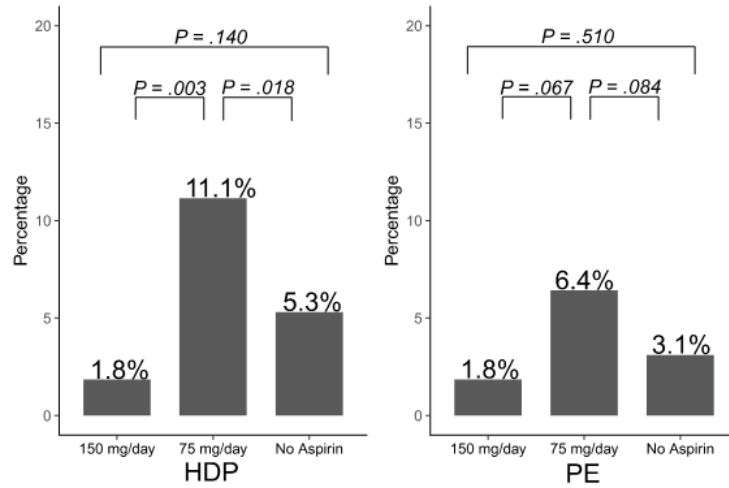


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