

## EFFECT OF LOW DOSE ASPIRIN IN PREVENTION OF PRETERM DELIVERY: A SKEPTICISM

Sidharth P.S.<sup>1</sup>, Aiswarya S.<sup>2</sup>, Prof. (Dr). Shaiju S. Dharan<sup>3</sup>, Dr. Dhanya Dharman\*

<sup>1,2</sup> Pharm. D Intern, Ezhuthachan College of Pharmaceutical Sciences.

<sup>3</sup> Principal/HOD, Ezhuthachan College of Pharmaceutical Sciences.

\* Associate Professor, Ezhuthachan College of Pharmaceutical Sciences.

Received on: 04/05/2023

Revised on: 25/05/2023

Accepted on: 15/06/2023

\*Corresponding Author

Dr. Dhanya Dharman

Associate Professor,

Ezhuthachan College of

Pharmaceutical Sciences.

### ABSTRACT

Low-dose aspirin use is still debated due to a lack of adequate clinical trials. Here we present our perspective on low-dose aspirin use in pregnancy and neonatal outcomes based on previous clinical trials. The effect of low-dose aspirin on preterm delivery needs to be clarified by the use of more appropriate participant inclusion criteria.

**KEYWORDS:** Aspirin, Preterm delivery, neonatal outcomes.

Preterm delivery is a leading cause of newborn morbidity and mortality. As per WHO rate of preterm birth ranges from 4-16%. In 2020 an estimated 13.4 million babies were delivered prematurely, and which resulted in 1 million deaths. It contributes to an array of chronic medical issues<sup>[1]</sup>. Low-dose aspirin is appealing as a potential preventive measurement against preterm birth since it is affordable, readily available, and has a respectable safety profile during pregnancy.<sup>[2]</sup> Reducing uterine contractility and inflammation via cyclooxygenase inhibition can prevent preeclampsia, small gestational age, placental insufficiency, and spontaneous premature birth.<sup>[3]</sup>

Only a few clinical trial data are available to help enlighten this field of practice. Women with a history of miscarriage at less than 20 weeks were randomly assigned to receive either 81mg of aspirin and folic acid or folic acid alone in a randomized control trial executed in Israel. Preterm birth rates were 4% with low-dose aspirin to 5.7% with placebo. In this randomized controlled experiment, the implication on the fetus was not explored.<sup>[4]</sup>

When compared to placebo, a multicenter study conducted in India, Kenya, Pakistan, Ghana, Congo, and Zambia found that low dose 81mg aspirin initiated between 6 weeks and 13 weeks and 6 days in nulliparous women between the age of 14 and 40 reduced preterm birth as well as fetal loss (stillbirth and abortion after 16 weeks). The likelihood of genetic and phenotypic variations among the trial participants could be the cause of the discrepancy in the result of the trials.<sup>[5]</sup> The APRIL STUDY was conducted in the Netherlands

in 26 hospitals. Women with singleton pregnancies and histories of spontaneous preterm birth between 22 and 37 weeks were assigned to receive 80mg aspirin between 8 weeks and 16 weeks of gestation which continued till 36 weeks of delivery. The study shows no significant effects on preterm labour by aspirin compared to placebo. This trial also shows composite poor neonatal outcomes in 4.6% of neonates of mothers on aspirin.<sup>[6]</sup>

The effects of aspirin on preterm delivery need to be clarified with more randomized trials especially with more randomized controlled trials especially focusing on a group of pregnant women sharing similar characteristics like age group, history of preterm labor before 37 weeks of gestation, comorbidities, and race. They should also need to answer if the treatment produces poor neonatal outcomes or not. Conducting clinical trials with emphasis on the above-mentioned aspects is complicated.

There is also skepticism about the dose of aspirin and the gestational period it needs to be started. The previous clinical trial mostly used 81mg and 80mg doses. The use of 75mg aspirin and its effect on preterm labour also remains uncertain and questionable. Randomized controlled trials fulfilling those aspects are required to answer if the use of low-dose aspirin could reduce preterm labour without poor neonatal outcomes.

### REFERENCES

1. Petrou S, Yiu HH, Kwon J. Economic consequences of preterm birth: a systematic review of the recent literature (2009–2017). Arch Dis Child., 2019;

- 104(5): 456–65. <https://doi.org/10.1136/archdischild.2018315778> PMID: 30413489.
2. Duley L, Henderson-Smart DJ, Meher S, King JF. Antiplatelet agents for preventing preeclampsia and its complications (review). The Cochrane Collaboration the CochraneLibrary, 2010; 10.
  3. Cadavid AP. Aspirin: the mechanism of action revisited in the context of pregnancy complications. *Frontiers in immunology*, Mar 15, 2017; 8: 261.
  4. Silver RM, Ahrens K, Wong LF, Perkins NJ, Galai N, Leshner LL, Faraggi D, Wactawski-Wende J, Townsend JM, Lynch AM, Mumford SL. Low-dose aspirin and preterm birth: a randomized controlled trial. *Obstetrics and Gynecology*, Apr, 2015; 125(4): 876.
  5. Hoffman MK, Goudar SS, Kodkany BS, Metgud M, Somannavar M, Okitawutshu J, Lokangaka A, Tshetu A, Bose CL, Mwapule A, Mwenechanya M. Low-dose aspirin for the prevention of preterm delivery in nulliparous women with a singleton pregnancy (ASPIRIN): a randomized, double-blind, placebo- controlled trial. *The Lancet*, Jan 25, 2020; 395(10220): 285-93.
  6. National Institute of Healthcare Excellence (NICE). Hypertension in pregnancy: diagnosis and management. NICE guideline 133. 2019 Jun 25 [cited 2021 Dec 30]. Available from: [www.nice.org.uk/guidance/ng133](http://www.nice.org.uk/guidance/ng133).
  7. Visser L, de Boer MA, de Groot CJ, Nijman TA, Hemels MA, Bloemenkamp KW, Bosmans JE, Kok M, van Laar JO, Sueters M, Scheepers H. Low dose aspirin in the prevention of recurrent spontaneous preterm labour—the APRIL study: a multicenter randomized placebo-controlled trial. *BMC pregnancy and childbirth*, Dec, 2017; 17: 1-7.
  8. Rolnik DL, Wright D, Poon LC, O’Gorman N, Syngelaki A, de MC, et al. Aspirin versus Placebo in Pregnancies at High Risk for Preterm Preeclampsia. *N Engl J Med.*, 2017; 377(7): 613–22. <https://doi.org/10.1056/NEJMoa1704559> PMID: 28657417.
  9. New Zealand Committee of The Royal Australian, New Zealand College of Obstetricians & Gynecologists (RANZCOG), New Zealand College of Midwives. Guidance regarding the use of low-dose aspirin in the prevention of pre-eclampsia. 2018 [cited 2021 Dec 30]. Available from: [https://ranzcog.edu.au/RANZCOG\\_SITE/media/RANZCOGMEDIA/New%20Zealand/Guidance-Aspirin-for-Prevention-of-Pre-eclampsia.pdf](https://ranzcog.edu.au/RANZCOG_SITE/media/RANZCOGMEDIA/New%20Zealand/Guidance-Aspirin-for-Prevention-of-Pre-eclampsia.pdf).
  10. World Health Organization. WHO recommendations for prevention and treatment of pre-eclampsia. Geneva, Switzerland: World Health Organization; 2011 [cited 2021 Dec 30]. Available from: [http://apps.who.int/iris/bitstream/10665/44703/1/9789241548335\\_eng.pdf](http://apps.who.int/iris/bitstream/10665/44703/1/9789241548335_eng.pdf).