Saudi Journal of Medicine

Abbreviated Key Title: Saudi J Med ISSN 2518-3389 (Print) | ISSN 2518-3397 (Online) Scholars Middle East Publishers, Dubai, United Arab Emirates Journal homepage: https://saudijournals.com

Original Research Article

Prevention of Preeclampsia in Saudi Arabia: Knowledge about Risk Factors and Aspirin Use among Obstetrical Care Physicians - A National Survey

Assem Alghamdi^{1*}, Jawaher Alkhaledi², Badi Albaqawi³

¹MD. MFM Consultant, Maternal Fetal Medicine Department at King Fahad Medical City in Riyadh, Saudi Arabia

²MFM Fellow, Maternal fetal medicine department at King Fahad Medical City in Riyadh, Saudi Arabia

³MFM Consultant, Maternal Fetal Medicine Department at King Fahad Medical City in Riyadh, Saudi Arabia

DOI: <u>10.36348/sjm.2024.v09i02.003</u> | **Received:** 30.11.2023 | **Accepted:** 07.01.2024 | **Published:** 02.02.2024

*Corresponding author: Assem Alghamdi

MD. MFM Consultant, Maternal Fetal Medicine Department at King Fahad Medical City in Riyadh, Saudi Arabia

Abstract

Objectives: To assess the level of awareness among obstetrical care providers about preeclampsia prevention including risk factors, good practice in aspirin prophylaxis, and to analyze the associated factors. Methods: A cross-sectional study conducted among gynecologists and obstetricians, maternal and fetal medicine specialists, and internal or family medicine physicians working in public or private care centers whom involved in obstetric care in Saudi Arabia. An onlineadministered questionnaire was designed to assess familiarity of aspirin role in prevention of preeclampsia and fetal growth restriction including proper dose, timing of intake, gestational age to start and discontinuation of treatment as well as the risk factors of PE among set of 13 conditions. An awareness score was calculated and divided into two levels: adequate and inadequate familiarity and knowledge. Practice in PE prevention and attitude towards aspirin use, in addition to participants' demographic and professional factors, were investigated and analyzed as profound factors. Results: Hundred sixty physicians were participated, 85% were obstetrician/gynecologists and 13.1 were maternal fetal medicine Specialists. Less than half of participants have adequate knowledge and awareness in aspirin role and a minority provided correct answers regarding the recommended aspiring dose, timing of intake, gestational age to start and discontinuation of treatment. However, knowledge about preeclampsia risk factors was relatively acceptable. Maternal fetal medicine specialist and physicians working in teaching hospitals were remarkably with better knowledge compared to their respective counterparts in primary and secondary centers. The existence of institutional guidelines about ASA use in pregnancy did not improve the knowledge level. Conclusion: The overall familiarity and knowledge in that regard was relatively poor, associating misconceptions about the risk factors and substantial gaps regarding the optimal timing and prescribing practice. Formal and continuous medical education curricula should be reviewed to promote good clinical practice in preeclampsia prevention as an essential dimension of maternal and fetal care.

Keywords: aspirin prophylaxis, Prevention of Preeclampsia, maternal and fetal medicine specialists, pregnancy.

Copyright © 2024 The Author(s): This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License (CC BY-NC 4.0) which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use provided the original author and source are credited.

Introduction

Preeclampsia constitutes the most common subtype of hypertensive disorders of pregnancy, which constitute the most common medical complication of pregnancy occurring in up to 10% of gestations [1,2]. In Saud Arabia, recent data indicate that 2.4% of parturient women develop hypertensive disorders of pregnancy, of whom 55% are preeclampsia [3]. Preeclampsia exposes to high maternal morbidity and mortality, as well as to poor fetal and neonatal outcomes including fetal growth restriction (FGR), preterm birth and still birth. Additionally, it is associated with increased incidence of

long-term complications, notably cardiovascular diseases in both the mother and infant, and congenital disorders such as neurodevelopmental disorders, bronchopulmonary dysplasia, and hematological complications [1,3–5].

Effective strategy to manage preeclampsia involves acting on three levels; prevention, early detection and effective treatment. In view of the burdensome morbidity and mortality, optimal management should be a fully integrative part of maternal preventive care and family planning [4].

Several risk factors for preeclampsia have been identified in the literature, enabling the establishment of preventive strategies based on the assessment of the level of risk [6]. Furthermore, a growing number of studied have examined the possibility that prophylactic use of lowdose acetylsalicylic acid (ASA), or aspirin, for the prevention of preeclampsia. The first randomized controlled trial that evidenced the efficacy of aspirin in reducing the risk of preeclampsia and FGR in high risk pregnancies was published in 1985 [7], and this effect has been thoroughly investigated and established thereafter, which led to aspirin prophylaxis of preeclampsia being increasingly recommended in various clinical and obstetrical profiles [8–12]. Consequently, several guidelines have emerged to provide an evidence-based framework for the identification of risk factors and the detection of highrisk pregnancies, and to define the good practice and prescribing rules in aspirin prophylaxis among at risk pregnancies [6,13-20].

In a perspective to assess the national level of maternal preventive care in term of preeclampsia, the present study was conducted to investigate the awareness and the knowledge level among obstetrical care physicians about the risk factors of preeclampsia and the familiarity of good practice in aspirin prophylaxis among high-risk women. It also explored the experience and attitude of the physicians in preeclampsia, as well as their use of and awareness about institutional or international guidelines. Such data would provide crucial indications for the preliminary measures to enhance the early detection and optimize the preventive management of preeclampsia, in order to reduce the associated morbidity and mortality.

METHOD

Design & Population

A cross-sectional study that was conducted among Saudi physicians dealing with obstetrical care. Obstetrician and gynecologists, maternal fetal medicine specialists, and internal or family medicine physicians working in public or private care centers in Saudi Arabia were included.

Tools

A structured questionnaire was designed to investigate the following dimensions: 1) practice and attitude towards aspirin prescribing among pregnant women, including multiple items such as effective experience in aspirin prescribing for the prevention of preeclampsia, existence of institutional guidelines for such indication, safety concerns of the physician, patient-reported side effects, etc. Table 2; 2) knowledge about prescribing aspirin for prevention of PE and FGR including proper dose, timing of intake, gestational age to start and to discontinue the treatment 3) conditions that may represent a risk of preeclampsia, which in turn constitute an indication for treatment with aspirin.

The questionnaire was completed with demographic and professional data of the participants including age, gender, province, type of practice (obstetrician/gynecologist, MFM specialist, other), level of practice (consultant, fellow, registrar, or resident), years in practice, type of hospital (academic, community, urban), level of maternal care at the participant's center (primary, secondary, tertiary).

Measurement of the Outcome

The outcome of interest of this study is the level of knowledge about the good clinical practice in prescribing ASA among pregnant women notably in the prevention of PE and FGR. A knowledge score was calculated based on participants' feedback in the questionnaire. Each correct answer was attributed the unitary score of 2 and 1, respectively. Thus, the total score (range 0-21) was calculated as the sum of unitary score. Afterwards, the knowledge level was categorized into adequate and inadequate by using the mean population's score as the cutoff.

Data Collection Procedure

An electronic version of the questionnaire was edited using SurveyMonkeyTM platform. The list and emails of all eligible physicians was acquired with the help of the MFM Saudi Group and Saudi Society of Obstetrics & Gynecology. A standard email was sent to all eligible participants including a brief presentation of the study objectives and relevance, a statement on the respect of the participant's confidentiality and right to withdraw from the survey as well as a statement about the respect of general ethics standards, and the link to the electronic survey form. In view of the small number of participations, several recalls and reminders were sent to increase the participation rate; these used a different email template to further promote the study. Responses were collected as an editable Excel sheet containing the final data of all participants.

Statistical Methods

The database was coded and edited for statistical analysis using the Statistical Package for Social Sciences version 21.0 for Windows (SPSS Inc., Chicago, IL, USA). Descriptive statistics were carried out to summarize the participants' demographic and professional factors as well as the patterns of answers to the different questionnaire's parts. Categorical variables are presented as frequency and percentage, while numerical variables are presented as mean ± standard deviation (SD). Pearson's Chi square test was used to analyze the association of the knowledge level with demographic and professional factors and attitudes towards aspirin; results are presented as the percentage of participants with adequate knowledge level within each category. A multivariate binary logistic model was carried out to analyze the independent factors of adequate knowledge; results are presented as odds ratio (OR) with 95% confidence interval (95%CI). A p value of <0.05 was considered to reject the null hypothesis.

RESULTS

Participants' Characteristics

Hundred sixty physicians responded to the survey, 120 (75.0%) were females, and majority (52.6%) were 40 years old or younger. The typical professional profile was a consultant (30.6%) or registrar (32.5%) obstetrician/gynecologist (85.0%) with 10 years practice or more (45.6%) in an academic hospital (75.0%). The regional distribution of the respondents showed predominant proportion from Riyadh (45.6%) and Makkah, western (33.8%) regions (Tables 1).

Practice in and attitude towards aspirin in the prevention of preeclampsia and FGR

All but 9 participants declared having already prescribed aspirin to their pregnant patients for the prevention of PE and FGR and 45.6% acknowledged having institutional guidelines for that indication. Regarding safety concerns, 19.4% stated that aspirin treatment comprises potential maternal or fetal side effects and 5.6% declared that aspirin prescribing is

commonly associated with side effects leading to treatment discontinuation by the patients. Most remarkably, majority physicians (53.7%) declared undergoing pressure from the patients or their family members to prescribe aspirin promptly, and 30.7% declared undergoing the same pressure from their seniors or the department heads. ACOG guideline were the most frequently followed guideline among the respondents (Table 2).

Knowledge about aspirin prescribing rules in the prevention of preeclampsia and FGR

A minority of participants (17.5%) provided the correct response regarding the proper dose (100-150 mg (17.5%) and recommended intake time (bedtime, 15.6%). Responses regarding the gestational age to start treatment with aspirin were variable, and only 36.9% correctly identified that it should be started before 16 weeks of pregnancy; however, 65.0% agreed that the treatment should discontinued not later than 36 weeks of pregnancy (Table 1).

Table 1: Participants' characteristics

Parameter	Category	Frequency	Percentage
Gender	Male	40	25.0
	Female	120	75.0
Age group (years)	<25	2	1.3
	25-30	30	18.8
	31-40	68	42.5
	41-50	34	21.3
	51-60	26	16.3
Type of practice	Obstetrician / Gynecologist	136	85.0
	Maternal-fetal Medicine Specialist	21	13.1
	Other	3	1.9
Level of practice	Consultant	49	30.6
	Fellow	14	8.8
	Registrar/Senior Registrar	52	32.5
	Resident	45	28.1
Years of practice	<5 years	44	27.5
	5-9 years	43	26.9
	>=10 years	73	45.6
Hospital type	Academic / Teaching	120	75.0
	Community	31	19.4
	Urban	9	5.6
Maternal care level	Primary	9	5.6
	Secondary	31	19.4
	Tertiary	120	75.0
Province	Riyadh	73	45.6
	Makkah	54	33.8
	AL Madinah	8	5.0
	Eastern region	16	10.0
	Southern region	3	1.9
	Prefer not to say	6	3.8

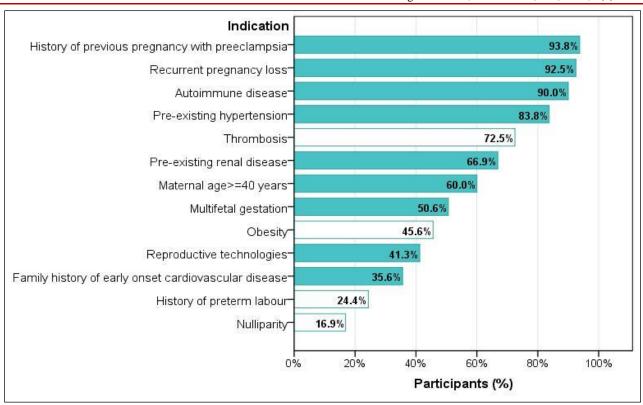
Table 2: Practice in and attitude towards aspirin in the prevention of preeclampsia and FGR

Item	Answering option	N	%
Have you ever prescribed ASA to your pregnant patients for the	No	9	5.6
prevention of preeclampsia?	Yes	151	94.4
Do you have a departmental or unit guideline with regards to	No	23	14.4
Aspirin usage in pregnancy for prevention of preeclampsia and	Yes	73	45.6
FGR?	Not sure	64	40.0
What specialists do you refer women at risk for preeclampsia to?	Obstetrician	94	58.8
	MFM specialist	42	26.3
	Internal Medicine	6	3.8
	None (no referral)	18	11.3
How frequent do your patients stop Aspirin due to the side effects	Rare	123	76.9
(stomach upset, bleeding etc.)?	Common	9	5.6
	Not sure	28	17.5
What would be your eventual safety concerns not recommending	Evidence not sufficient	15	9.4
ASA to your patients for preeclampsia prevention?	Potential maternal SE	26	16.3
	Potential fetal SE	5	3.1
	None	114	71.3
Do you receive pressure from patients or their family members to	No	74	46.3
prescribe Aspirin promptly?	Yes	25	15.6
	Sometimes	61	38.1
Do you receive pressure from your seniors or department to	No	111	69.4
prescribe Aspirin promptly?	Yes	14	8.8
	Sometimes	35	21.9
Which guidelines do you follow?	ACOG 2016	87	54.4
•	ACOG 2013	8	5.0
	SOGC 2012	3	1.9
	NICE	32	20.0
	None of the above	30	18.8
FGR: fetal growth restriction; MFM: Maternal-fetal Medicine; SE:	side effects;	-	•

Regarding the indications of aspirin use in that regards, history of previous preeclampsia (93.8%), recurrent pregnancy loss (92.5%) autoimmune diseases (90.0%) and preexisting hypertension (83.8%) were the more frequently identified appropriate indications; whereas thrombosis (72.5%), obesity (45.6%) and history of preterm labor (24.4) were the most frequently mistaken indications. Of note less than 50% of the participants identified the use of reproductive technologies (41.3%) and history of heart diseases (35.6%) as indications for aspirin among pregnant women (Figure 1).

Levels and factors of knowledge about aspirin use in the prevention of preeclampsia and FGR

The histogram of raw knowledge scores is depicted in Figure 2, and mean±SD score was 11.25±2.81 (range=2, 19). By considering knowledge level ≥ mean as a cutoff to define adequate knowledge, the percentage of patients with adequate knowledge was 42.5%. Factors associated with knowledge level are depicted in Table 4. These showed higher percentage of participants with adequate knowledge in the age group 31-40 (p<0.001), fetal medicine specialist (p=0.004), fellows (p=0.029), participants with 5-9 years of practice (p<.001), and those practicing in an academic or teaching hospital (p=0.003), by reference to their counterparts. No association of knowledge level was observed with gender, province, physician's safety concerns, awareness about institutional guidelines and the guidelines followed by the participants.



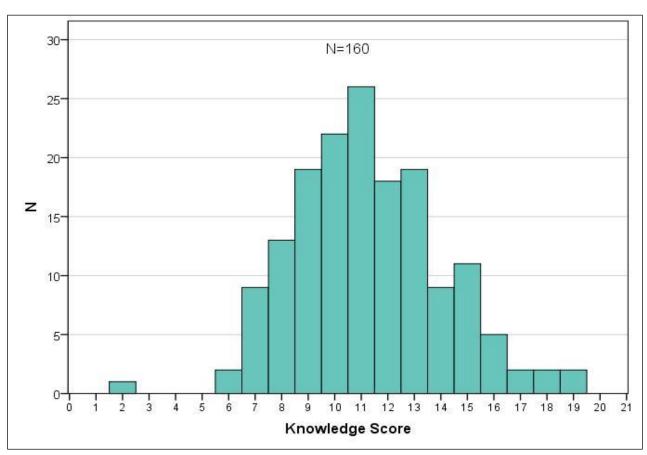


Table 3: Knowledge about aspirin prescribing rules in the prevention of preeclampsia and FGR

Item	Answering option	N	%
What dose of ASA you prescribe for the prevention of preeclampsia?	81 mg	126	78.8
	100 mg	28	17.5
	162 mg	6	3.8
At what specific time of day do you recommend ASA to be taken for the	Morning	16	10.0
prevention of preeclampsia?	After meals	38	23.8
	Bedtime	25	15.6
	Not sure	81	50.6
If you are starting aspirin for prevention of preeclampsia or FGR, when is your	Before pregnancy	15	9.4
recommended time to begin?	4-6 weeks	37	23.1
	1 st semester (<12 weeks)	29	18.1
	Before 16 weeks	59	36.9
	No GA preference	3	1.9
	Anytime seen in clinic	17	10.6
If your patient is taking ASA for preeclampsia prevention, when do you	34 weeks	29	18.1
recommend, she stop taking ASA?	36 weeks	104	65.0
	At delivery	24	15.0
	Not sure	3	1.9

Table 4: Factors associated with the level of knowledge about aspirin use in the prevention of preeclampsia and fetal growth restriction.

Factor	Category	N (100%)	% adequate knowledge	p-value
Gender	Male	40	37.5	
	Female	120	44.2	.460
Age group (years)	<25	2	100.0	
	25-30	30	26.7	
	31-40	68	60.3	
	41-50	34	32.4	
	51-60	26	23.1	<.001*
Type of practice	Obstetrician / Gynecologist	136	37.5	
	MFM Specialist	21	76.2	
	Other	3	33.3	.004*
Level of practice	Consultant	49	40.8	
	Fellow	14	78.6	
	Registrar/Senior Registrar	52	42.3	
	Resident	45	33.3	.029*
Years of practice	<5 years	44	31.8	
-	5-9 years	43	74.4	
	>=10 years	73	30.1	<.001*
Hospital type	Academic / Teaching	120	49.2	
	Other	40	22.5	.003*
Maternal care level	Primary	9	11.1	
	Secondary	31	54.9	
	Tertiary	120	41.7	.061
Province	Riyadh	73	47.9	
	Makkah	54	37.0	
	Other	33	39.4	.433
Institutional guidelines	No	23	43.5	
	Yes	73	42.5	
	Not sure	64	42.2	.994
Eventual concerns about aspirin	Evidence not sufficient	15	20.0	
	Potential maternal SE	26	38.5	
	Potential fetal SE	5	20.0	
	None	114	47.4	.143
Guidelines followed	ACOG 2016	87	44.8	
	ACOG 2013	8	25.0	
	SOGC 2012	3	66.7	
	NICE	32	34.4	
	None of the above	30	46.7	.560

Test used: chi square test; * statistically significant result (p<0.05);

Table 5: Independent factors associated with adequate knowledge about aspirin use in the prevention of preeclampsia and fetal growth restriction.

precedingsia and retail growth restriction.						
Predictor	Category	OR	95%CI		p-value	
Age group (years)	≤30	1.65	0.30	8.89	.779	
	31-40	1.47	0.47	4.67	.563	
	>40	Ref	-	-	.509	
Type of practice	MFM Specialist	6.89	1.65	28.75	.008*	
	Other	Ref	-	-	-	
Level of practice	Consultant Registrar	Ref	-	-	.844	
	Resident	1.48	.39	5.58	.561	
	Fellow	1.03	.21	5.05	.971	
Years of practice	<5 years	0.42	0.09	1.99	.272	
	5-9 years	4.65	1.41	15.41	.012*	
	>=10 years	Ref	-	-	.001*	
Hospital type	Academic / Teaching	3.62	1.37	9.56	.009*	
	Other	Ref	-	_	_	

Multivariate binary logistic regression; dependent variable (value): knowledge level (adequate); * statistically significant result (p<0.05).

Independent factors of knowledge

The multivariate regression model showed that adequate knowledge was independently associated with maternal fetal medicine specialty (OR=6.89, p=0.008), practice in an academic or teaching hospital (OR=3.62, p=0.009), and those having 5-9 years of practice (OR=4.65, p=0.012) (**Table 5**).

DISCUSSION

Summary of Findings

This national survey explored an important dimension of the maternal preventive care and demonstrated that the use of ASA in the prevention of preeclampsia is limited by inadequate levels of knowledge and practice among the obstetrical care providers. Less than half participants had adequate knowledge defined by a score >11 out of 21 and a minority were knowledgeable of the recommended dose, timing, and time of start of treatment with ASA. Further, knowledge was inconsistent about pregnancy conditions that constitute preventive indications for ASA. Nevertheless, knowledge level was remarkably higher among maternal fetal medicine specialists, in teaching hospitals and among participants aged 31-40 years and having 5-9 years of practice suggesting a generational effect. On the other hand, the existence of institutional guidelines about ASA use in pregnancy did not improve the knowledge level.

Obstetrician's knowledge and practice in preeclampsia prevention

The present study focused on the preventive care of preeclampsia, as enhancing the prevention includes efficient screening and identification of highrisk pregnancies and timely initiation of the prophylaxis. The overall knowledge level of obstetricians was relatively poor, associating substantial gap of knowledge about the dose and circadian time of aspirin administration, as well as about the gestational age where prophylaxis should be started. However, MFM

specialists showed significantly better knowledge, indicating a better management in MFM centers of this category of patients. These findings are comparable to a study by Snead et al., which showed that MFM specialists had an overall practice in preeclampsia that is better that other obstetricians, including the gestational age when aspirin is be started. Of note, the study highlighted that MFM specialists were more likely to use an algorithm for the management of preeclampsia, compared to their counterparts (21). This indicates the need for reviewing the academic curricula for obstetricians and gynecologists as well as for family physicians, by enhancing education on preeclampsia. Another expected observation is the substantial variance of knowledge between academic hospitals and nonacademic care centers, which further highlights the importance of training and clinical exposure in improving knowledge and practice.

Aspirin prophylaxis in PE: Rationale and recommendations

Attitudes among obstetrical care physicians in the present study showed that majority (~55%) were not aware of or do not have departmental or institutional guidelines for the use of aspirin prophylaxis in preeclampsia and FGR, and nearly 10% believed there is no strong evidence for the efficacy of such treatment. On the other hand, over 80% declared following international guidelines, mainly ACOG and NICE guidelines, while 20% recognized not following any guidelines. This denotes the lack of standard care in the national level and highlights the urgent need to harmonize both training and practice across the different institutions and obstetric care providers in the light of the cumulative evidence. While some controversies remain regarding the indications and modalities of aspirin prescribing in the prevention of PE and FGR, there is consensus regarding its beneficial effect (8–12).

Further, the mechanisms of action of aspirin in preeclampsia are rationalized by early studies showing a

repressive effect on platelet thromboxane production due to its COX-1 inhibitor effect, and the regulation of angiotensin II sensitivity that characterizes preeclampsia, in addition to a proangiogenic effect (22–24). All these effects, besides other more recently demonstrated effects, result in improved trophoblast invasion and restored placental arterial flow, thus reducing the placental hypoxia and breaking the vicious cycle of oxidative stress inflammation, and endothelial dysfunction that underlies preeclampsia (25-29). Clinically, several randomized clinical trials and metaanalysis have confirmed the beneficial effect of low-dose aspirin in reducing the overall incidence of preeclampsia and severe preeclampsia, as well as the associated obstetrical and fetal complications such as preterm birth, intrauterine growth restriction, perinatal death and highrisk pregnancy (9,30).

Consequently, several recommendations have been issued to indicate the use of aspirin in preeclampsia based on a risk stratification approach. Among these recommendations are those established by the US. Preventive Services Task Force (USPSTF) guidelines (13), the American College of Obstetricians and Gynecologists (ACOG) (14), the World Health Organization (15), the National Institute of Health and Care Excellence (NICE) (16), and the American Heart Association (17).

Knowledge about preeclampsia risk factors

Despite the lack of consensus regarding the risk evaluation across these different guidelines, several risk factors have been consistently identified and classified into high and moderate risk of preeclampsia. History of preeclampsia, multifetal gestation, diabetes (both types), chronic hypertension, renal diseases and autoimmune diseases, such as systemic lupus erythematous and antiphospholipid syndrome, are considered high risk factors. On other hand, nulliparity, obesity, family history of preeclampsia, older maternal age, and being of some ethnic descents are considered moderate risk factors [6,13].

In the present study, awareness levels about risk factors such as nulliparity and obesity were inadequate, which exposes to the risk of undertreatment and mismanagement of a number at risk pregnancies. This emphasizes the relevance of implementing guidelines at the institutional level, and regularly auditing the adherence to these guidelines among the physicians. Literature shows that the implementation of such recommendations and guidelines have enabled reduction of the incidence of preeclampsia, such as the case of the US. Preventive Services Task Force guidelines which was associated with 30% drop in the incidence of recurrent preeclampsia among women with a positive preeclampsia history [31].

Knowledge about aspirin prescribing rules

Majority participants in the present study agreed that aspirin prophylaxis should be initiated early pregnancy; however only approximately correctly identified the optimal gestation age, which is 16 weeks. This timing is recommended based on the meta-analysis of randomized trial, by Bujold et al., which demonstrated that the initiation of aspirin prophylaxis before 16 weeks of gestation was associated with 53% and 56% reduction of the relative risk of developing preeclampsia and FGR, respectively, while no significant risk reduction was observed in case of later initiation [18]. This was confirmed by another meta-analysis showing 47% versus 19% reduction of preeclampsia in case of early (before 16 weeks) versus late (after 16 weeks) initiation of aspirin respectively, besides 53% reduction of severe preeclampsia and 46% reduction of FGR. The same study demonstrated that higher doses, i.e. 100 and 150 mg, were associated with greater effect [19]. Regarding the time when aspirin prophylaxis should be stopped, nearly two-third participants correctly identified that it should be continued to the 36th week of gestational age. Indeed, this timing is in accordance with the NICE guidelines and corresponds to the cutoff gestational age, above which the induction of labor is safest [6,16]. Only one-third participants (36.9%) correctly identified bedtime as the optimal circadian time for ASA intake. It was previously demonstrated in a double-blind randomized trial that aspiring given before bedtime was associated with significant reduction of blood pressure among pregnant women, compared to placebo, while a lesser effect was observed when given 8 hours after awakening and no effect when given on awakening. Authors of the trial concluded to efficacy of aspirin in the prevention of preeclampsia being conditioned by the timed use [20].

Eventual limitations of guidelines implementation and further considerations

health perspective, In a public implementation of recommendations for aspirin prophylaxis may have some limitations that should be mentioned. A study evaluated the NICE and USPSTF guidelines for identifying pregnancies at high risk of preeclampsia. Results showed that the two guidelines had comparable screening performance including poor sensitivity (13-14%) and very high specificity (~96%) [32]. These observations may indicate the limited interest of these guidelines at the population level and suggest their use with caution. On the other hand, a costeffectiveness study using Monte Carlo simulations showed that universal use of aspirin among pregnant women, without risk stratification, would be more costeffective in over 90% simulations, by reference to aspirin prophylaxis in accordance with the US. Preventive Services Task Force guidelines or based on biomarkers and ultrasound screening [33]. Furthermore, high-risk patients who benefit from timely aspirin prophylaxis are not exempted from developing preeclampsia; a marginal risk remains notably in patients having diabetes or

elevated diastolic blood pressure prior to treatment initiation, both being demonstrated to be independent risk factors for preeclampsia, besides other risk factors such as obesity, history of preeclampsia hypertension [34]. Other dimensions to be considered aspirin prophylaxis are aspirin responsiveness or resistance and patients' adherence, both being associated with reduced efficacy [35]. Patient's knowledge and awareness constitutes a key contributor in a successful prevention strategy and should be promoted among all obstetrical care providers, targeting specifically women with history or risk of preeclampsia [6,16].

Study Limitations

The major limitation of this national survey is the low participation rate, which prevents from generalizing the findings and drawing solid conclusions. Further studies should be carried out to assess the levels of knowledge and practice in the prevention of preeclampsia at the national level to determine the related gaps and design the appropriate corrective measures.

CONCLUSION

This national study showed that the prevention of preeclampsia is limited by inadequate levels of knowledge and practice among the obstetrical care providers in Saudi Arabia. The overall knowledge level of obstetricians was relatively poor, associating misconceptions about the risk factors and substantial gaps regarding the optimal timing and prescribing practice. We note the inconsistent use of institutional guidelines in the prevention of preeclampsia and the lack of standardized practice, urging for the implementation of national guidelines. Besides, formal and continuous medical education curricula should be reviewed to promote good clinical practice in preeclampsia prevention as an essential dimension of maternal and fetal care. Further awareness raising programs should target the patients, to enhance screening and early identification of high- risk pregnancies and promote patients' adherence to an eventual aspiring prophylaxis. Preeclampsia is a deadly condition that should be managed as a public health issue.

Conflict of Interest: none

REFERENCES

- 1. Eiland, E., Nzerue, C., Faulkner, M. Preeclampsia. (2012). Journal of Pregnancy [Internet]. 2012;2012:1–7. Available from: http://www.hindawi.com/journals/jp/2012/586578/
- 2. Lai, C., Coulter, S.A. & Woodruff, A. Hypertension and Pregnancy. (2017). *Texas Heart Institute Journal* [Internet]. 44(5):350–1. Available from: https://meridian.allenpress.com/thij/article/44/5/350/85349/Hypertension-and-Pregnancy
- 3. Subki, A. H., Algethami, M. R., Baabdullah, W. M., Alnefaie, M. N., Alzanbagi, M. A., Alsolami, R. M.,

- & Abduljabbar, H. S. (2018). Prevalence, risk factors, and fetal and maternal outcomes of hypertensive disorders of pregnancy: a retrospective study in Western Saudi Arabia. *Oman medical journal*, 33(5), 409.
- Backes, C. H., Markham, K., Moorehead, P., Cordero, L., Nankervis, C. A., & Giannone, P. J. (2011). Maternal preeclampsia and neonatal outcomes. *Journal of pregnancy*, 2011.
- 5. Steegers, E. A., Von Dadelszen, P., Duvekot, J. J., & Pijnenborg, R. (2010). Pre-eclampsia. *The Lancet*, *376*(9741), 631-644.
- English, F. A., Kenny, L. C., & McCarthy, F. P. (2015).
 Risk factors and effective management of preeclampsia. *Integrated blood pressure control*, 7-12.
- 7. Beaufils, M., Donsimoni, R., Uzan, S., & Colau, J. C. (1985). Prevention of pre-eclampsia by early antiplatelet therapy. *The Lancet*, *325*(8433), 840-842.
- 8. Roberge, S., Odibo, A. O., & Bujold, E. (2016). Aspirin for the prevention of preeclampsia and intrauterine growth restriction. *Clinics in laboratory medicine*, *36*(2), 319-329.
- 9. Roberge, S., Villa, P., Nicolaides, K., Giguère, Y., Vainio, M., Bakthi, A., ... & Bujold, E. (2012). Early administration of low-dose aspirin for the prevention of preterm and term preeclampsia: a systematic review and meta-analysis. *Fetal diagnosis and therapy*, 31(3), 141-146.
- Magee, L. A., Pels, A., Helewa, M., Rey, E., von Dadelszen, P., Audibert, F., ... & Sebbag, I. (2014). Diagnosis, evaluation, and management of the hypertensive disorders of pregnancy: executive summary. *Journal of Obstetrics and Gynaecology Canada*, 36(5), 416-438.
- 11. Ayala, N. K., & Rouse, D. J. (2019). A nudge toward universal aspirin for preeclampsia prevention. *Obstetrics & Gynecology*, *133*(4), 725-728.
- Poon, L. C., Wright, D., Rolnik, D. L., Syngelaki, A., Delgado, J. L., Tsokaki, T., ... & Nicolaides, K. H. (2017). 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. *American journal of obstetrics and gynecology*, 217(5), 585-e1.
- 13. LeFevre, M. L., & US Preventive Services Task Force*. (2014). Low-dose aspirin use for the prevention of morbidity and mortality from preeclampsia: US Preventive Services Task Force recommendation statement. *Annals of internal medicine*, 161(11), 819-826.
- 14. Obstetricians ACo, G. (2013). Hypertension in pregnancy. Report of the American college of obstetricians and gynecologists' task force on hypertension in pregnancy. *Obstet gynecol*, 122(5), 1122.
- 15. World Health Organization. WHO recommendations for prevention and treatment of pre- eclampsia and eclampsia [Internet]. Geneva; 2011. Available from: http://whqlibdoc.who.int/publications/2011/978924 1548335_eng.pdf

- Redman CWG. Hypertension in pregnancy: the NICE guidelines. Heart (British Cardiac Society) [Internet]. 2011 Dec;97(23):1967–9. Available from:
 - http://www.ncbi.nlm.nih.gov/pubmed/21990386
- 17. Bushnell, C., McCullough, L. D., Awad, I. A., Chireau, M. V., Fedder, W. N., Furie, K. L., ... & Walters, M. R. (2014). Guidelines for the prevention of stroke in women: a statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*, 45(5), 1545-1588.
- Bujold, E., Roberge, S., Lacasse, Y., Bureau, M., Audibert, F., Marcoux, S., ... & Giguere, Y. (2010). Prevention of preeclampsia and intrauterine growth restriction with aspirin started in early pregnancy: a meta-analysis. *Obstetrics & Gynecology*, 116(2 Part 1), 402-414.
- 19. Roberge, S., Nicolaides, K., Demers, S., Hyett, J., Chaillet, N., & Bujold, E. (2017). The role of aspirin dose on the prevention of preeclampsia and fetal growth restriction: systematic review and meta-analysis. *American journal of obstetrics and gynecology*, 216(2), 110-120.
- 20. Hermida, R. C., Ayala, D. E., & Iglesias, M. (2003). Administration time–dependent influence of aspirin on blood pressure in pregnant women. *Hypertension*, *41*(3), 651-656.
- Snead, C. M., Strassberg, E., Overcash, R., Stark, L., Paglia, M. J., Schulkin, J., & Jelin, A. (2020). Obstetricians' knowledge and practices regarding the management of preeclampsia. *The Journal of Maternal-Fetal & Neonatal Medicine*, 33(17), 2970-2975.
- 22. Benigni, A., Gregorini, G., Frusca, T., Chiabrando, C., Ballerini, S., Valcamonico, A., ... & Remuzzi, G. (1989). Effect of low-dose aspirin on fetal and maternal generation of thromboxane by platelets in women at risk for ppregnancy-induced hypertension. *New England Journal of Medicine*, 321(6), 357-362.
- 23. SIBAI, B. M., MIRRO, R., CHESNEY, C. M., & LEFFLER, C. (1989). Low-dose aspirin in pregnancy. *Obstetrics & Gynecology*, 74(4), 551-557.
- 24. Dekker, G. A., & Sibai, B. M. (1993). Low-dose aspirin in the prevention of preeclampsia and fetal growth retardation: rationale, mechanisms, and clinical trials. *American journal of obstetrics and gynecology*, 168(1), 214-227.
- 25. Su, M. T., Wang, C. Y., Tsai, P. Y., Chen, T. Y., Tsai, H. L., & Kuo, P. L. (2019). Aspirin enhances trophoblast invasion and represses soluble fms-like tyrosine kinase 1 production: a putative mechanism

- for preventing preeclampsia. *Journal of hypertension*, 37(12), 2461-2469.
- Loussert, L., Vidal, F., Parant, O., Hamdi, S. M., Vayssiere, C., & Guerby, P. (2020). Aspirin for prevention of preeclampsia and fetal growth restriction. *Prenatal diagnosis*, 40(5), 519-527.
- 27. Redman, C. W., & Sargent, I. L. (2005). Latest advances in understanding preeclampsia. *Science*, 308(5728), 1592-1594.
- 28. Sánchez-Aranguren, L. C., Prada, C. E., Riaño-Medina, C. E., & Lopez, M. (2014). Endothelial dysfunction and preeclampsia: role of oxidative stress. *Frontiers in physiology*, *5*, 372.
- 29. Cadavid, A. P. (2017). Aspirin: the mechanism of action revisited in the context of pregnancy complications. *Frontiers in immunology*, 8, 261.
- 30. Xu, T. T., Zhou, F., Deng, C. Y., Huang, G. Q., Li, J. K., & Wang, X. D. (2015). Low-Dose aspirin for preventing preeclampsia and its complications: a meta-analysis. *The Journal of Clinical Hypertension*, 17(7), 567-573.
- Tolcher, M. C., Chu, D. M., Hollier, L. M., Mastrobattista, J. M., Racusin, D. A., Ramin, S. M., ... & Aagaard, K. M. (2017). Impact of USPSTF recommendations for aspirin for prevention of recurrent preeclampsia. *American journal of obstetrics and gynecology*, 217(3), 365-e1.
- 32. Al-Rubaie, Z. T., Askie, L. M., Hudson, H. M., Ray, J. G., Jenkins, G., & Lord, S. J. (2018). Assessment of NICE and USPSTF guidelines for identifying women at high risk of pre-eclampsia for tailoring aspirin prophylaxis in pregnancy: an individual participant data meta-analysis. *European Journal of Obstetrics & Gynecology and Reproductive Biology*, 229, 159-166.
- 33. Mallampati, D., Grobman, W., Rouse, D. J., & Werner, E. F. (2019). Strategies for prescribing aspirin to prevent preeclampsia: a cost-effectiveness analysis. *Obstetrics & Gynecology*, *134*(3), 537-544.
- 34. Block-Abraham, D. M., Turan, O. M., Doyle, L. E., Kopelman, J. N., Atlas, R. O., Jenkins, C. B., ... & Baschat, A. A. (2014). First-trimester risk factors for preeclampsia development in women initiating aspirin by 16 weeks of gestation. *Obstetrics & Gynecology*, 123(3), 611-617.
- 35. Shanmugalingam, R., Wang, X., Motum, P., Fulcher, I., Lee, G., Kumar, R., ... & Makris, A. (2020). Clinical influence of nonadherence with prophylactic aspirin in preventing preeclampsia in high-risk pregnancies: a multicenter, prospective, observational cohort study. *Hypertension*, 75(4), 1125-1132.