Advanced Maternal Age and the Frequency of Pre-Eclampsia - A Single-Center Cross Sectional Study from Saudi Arabia

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ABSTRACT

BACKGROUND

Pregnancy at advanced maternal age (≥ 35 years) has become very common worldwide. Pre-eclampsia (PE) is a serious complication of hypertensive pregnancy that is associated with considerable morbidity and mortality to both the mother and foetus/newborn. This research aimed to inspect the prevalence of PE in a single hospital located in Jeddah, Saudi Arabia, and examine the influence of advanced maternal age (≥ 35 years) on the occurrence of PE in singleton deliveries.

METHODS

A retrospective study (January 2011 to December 2018) was carried out at King Abdulaziz University Hospital (KAUH), located in Jeddah, Saudi Arabia. Categorical variables were evaluated with χ^2 test. Odds ratio (OR) with 95% confidence intervals (95% CI) was used to estimate the comparative risk of developing PE (the outcome variable) according to the maternal age (the exposure variable) at the time of pregnancy.

RESULTS

During the study period, 3942 singleton deliveries occurred at KAUH. The demographic characteristics (age and PE) of the study population are summarized in Table 1. Overall, there were 2426 deliveries with a maternal age < 34 years (61.5%), whereas there were 1516 deliveries with a maternal age ≥ 35 years (38.5%). Only 167 deliveries had a diagnosis of PE, thus yielding an overall prevalence of 4.2% in this retrospective study. The percentages of PE cases in patients with maternal age < 34 years and ≥ 35 years were 3.7% and 5.1%, respectively. Two-tailed Chi-square test of independence showed that there was a statistical significance between advanced maternal age and occurrence of PE ($p=0.02$). To examine the comparative risk of developing PE with relation to the maternal age, an OR analysis showed that patients with advanced maternal age (≥ 35 years) were 1.4 times more likely to develop PE during gestation when compared to patients with < 34 years, and this comparative risk was substantial (OR: 1.4, 95% CI: 1.1-1.9, $p=0.03$).

CONCLUSIONS

The low prevalence of PE (3.9%) in our study was largely in agreement with the published regional and international figures. Advanced maternal age (≥ 35 years) is a statistically significant factor for developing PE during pregnancy.

KEY WORDS

Incidence, Prevalence, Pre-Eclampsia, Advanced Maternal Age, Saudi Arabia

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BACKGROUND

Pregnancy at advanced maternal age has become very common worldwide, including the developed and developing countries over the past few decades.^[1-3] Reasons for delayed childbearing and motherhood are multifactorial and may be attributable to a wide array of personal, cultural, social, biological and economic factors.^[4] The literature is conflicted on the age cut-off for advanced maternal age; however, the most commonly accepted consensus for advanced maternal age is 35 years or older.^[5] Others specify "very" advanced maternal age as 40 years or older,^[6] or 45 years or older.^[7,8]

Pregnancy at advanced maternal age (≥ 35 years) is hardly ever without threats to the mother and foetus/newborn.^[3] Accumulating evidence from high-quality systematic reviews and meta-analyses of several studies have established links between advanced maternal age and adverse pregnancy results. Such outcomes are enormous and comprise foetal loss (for example, miscarriage and still-birth), hypertensive disorders (for example, eclampsia, pre-eclampsia (PE) and gestational hypertension), abnormal newborn growth, placental abnormalities (for example, placenta previa and placenta abruptio), preterm labour (spontaneous or iatrogenic), gestational diabetes mellitus and Caesarean section (elective or emergency).^[3,9-14]

PE is a common hypertensive condition of pregnancy worldwide. PE is characterized by the presence of new-onset hypertension and proteinuria plus/minus multi-organ dysfunction taking place after 20 weeks of gestation.^[15] It is regarded as a serious complication of pregnancy that is associated with considerable morbidity and mortality to both the mother and foetus/newborn.^[15] Positive risk factors for PE are abundant and include, but not limited to, advanced maternal age, family history of PE, nulliparity, multiple pregnancy, molar pregnancy and maternal comorbidities (for example, diabetes mellitus, obesity, chronic hypertension and chronic kidney disease).^[16]

Advanced maternal age (≥ 35 years) constitutes a substantial influential factor implicated in adverse pregnancy outcomes generally,^[2] and in PE specifically.^[3,10,16,17] Thus, the knowledge of this population-based risk factor is of great value in the childbearing decision-making for both patients (that is, the mothers with advanced maternal age) and the managing physicians.

To the best of our knowledge, from Saudi Arabia, there is a few number of studies which endeavoured to estimate the prevalence of PE among pregnant women.^[2,18-23] Moreover, only half of these studies attempted to directly inspect the link between advanced maternal age and the occurrence of PE.^[2,8,20] Such epidemiological studies are warranted to withdraw concrete population-specific conclusions pertaining to the prevalence of PE in Saudi Arabia and its relationship to advanced maternal age.

Thus, the task of this research is two folds: (i) to estimate the frequency of PE in a single hospital located in the Jeddah, Saudi Arabia, and (ii) to examine the influence of advanced maternal age (≥ 35 years) on the frequency of PE.

METHODS

The cross-sectional study was carried out at King Abdulaziz University Hospital (KAUH), located in Jeddah, Saudi Arabia. The research procedure was cleared by the Research Ethics Board (Reference: 361-19).

From 01-January-2011 to 31-December-2018, the number of all singleton deliveries was identified. Afterward, the respective electronic medical records were retrospectively analysed for two demographical data including maternal age and the occurrence of PE.

The diagnosis of PE was established in line with the guidelines of ISSHP, which stands for the International Society for the Study of Hypertension in Pregnancy.^[24]

The research inclusion criteria consisted of: (i) maternal age of greater than or equal to 18 years, (ii) singleton pregnancy, and (iii) confirmed diagnosis of PE. The research exclusion criteria consisted of: (i) maternal age less than or equal to 17 years, (b) non-singleton pregnancy, and (iii) incomplete data about maternal age and occurrence of PE.

The primary two tasks of this research are: (i) to explore the prevalence of PE, and (ii) to scrutinize the link between advanced maternal age (≥ 35 years) and frequency of PE. To that end, pregnant women were dichotomized into two sets of patients: (i) < 34 years, and (ii) ≥ 35 years. In this study, the age cut-off for advanced maternal age of 35 years was in line with the most commonly accepted consensus for advanced maternal age.^[5]

Data were analysed using the SPSS software. A p value less than 0.05 was counted as significant statistically. χ^2 test was used to compare categorical variables. Odds ratios (OR) with 95% confidence intervals (95% CI) was used to estimate the comparative risk of developing PE (the outcome variable) according to the maternal age (the exposure variable) at the time of pregnancy.

RESULTS

During the study period, 3942 singleton deliveries occurred at KAUH. Overall, there were 2426 deliveries with a maternal age < 34 years (61.5%), whereas there were 1516 deliveries with a maternal age ≥ 35 years (38.5%). Only 167 deliveries had a diagnosis of PE, thus yielding an overall prevalence of 4.2% in this retrospective study. The percentages of PE cases in patients with maternal age < 34 years and ≥ 35 years were 3.7% and 5.1%, respectively.

Two-tailed Chi-square test of independence showed that there was a statistical significance between advanced maternal age and occurrence of PE ($p=0.02$). To examine the comparative risk of developing PE (the outcome variable) with relation to the maternal age (the exposure variable), an odds ratio (OR) analysis showed that patients with advanced maternal age (≥ 35 years) were 1.4 times more likely to develop PE during gestation when compared to patients with < 34 years, and this comparative risk was substantial (OR: 1.4, 95% CI: 1.1-1.9, $p=0.03$).

References	Authors	Year	Region of Saudi Arabia	Prevalence of Pre-Eclampsia
[19]	Al-Ghamdi et al.	1999	Northwest	1.9%*
[18]	Lawoyin et al.	1996	Northwest	2.8%
[20]	Al-Mulhim et al.	2003	East	2.5%
[21]	Sobande et al.	2007	Southwest	0.9%†
[22]	Wahabi et al.	2016	Central	1.1%
[2]	Fayed et al.	2017	Central	1.1%
[23]	Subki et al.	2018	West	1.3%
Present study	Abu-Zaid et al.	2020	West	4.3%

Table 1. Studies that Reported the Frequency of Pre-Eclampsia in Saudi Arabia

* Frequency rate includes the combined frequency of pre-eclampsia and eclampsia.

† Frequency rate includes only the frequency of "severe" pre-eclampsia.

DISCUSSION

Hypertensive disorders of pregnancy (HDP) are commonly encountered in the antenatal clinics, and they are estimated to complicate 10% of all gestations.^[25] HDP comprise four subcategories, namely, gestational hypertension, PE, chronic hypertension and chronic hypertension with superimposed PE.^[15]

PE carries on to be a chief root of morbidity and mortality to pregnant women and their newborn.^[15] The precise underlying pathogenesis of PE remains unknown.^[26] Nevertheless, contemporarily, PE is largely understood as a disorder of placental insufficiency and generalized endothelial dysfunction.^[26] Early-onset/'placental' and late-onset/'maternal' PE happen before 34 and after 34 weeks of gestation, respectively.^[27]

Worldwide, the estimated incidence of PE is 4-5%.^[28] Our study demonstrated that the incidence of PE was 4.2%. This figure was in accordance with the published literature from Saudi Arabia (Table 1).^[2,18-23] The numerical differences observed in the incidence rates of PE can be ascribed to several factors, such as the differences in the populations studied and heterogeneity in the study design. To elaborate, Al-Ghamdi et al.^[19] found that the frequency of both PE and eclampsia was 1.9% without differentiating the specific proportions of each disorder in their study. Contrariwise, Sobande and friends.^[21] reported only the incidence of patients who were diagnosed with 'severe' PE which amounted to 0.9%.

In our study, twin pregnancies were excluded from the study analysis for two reasons. First, we wanted to have a uniform (controlled) study population with regard to singleton pregnancy versus non-singleton pregnancy. Second, twin pregnancies have been shown to intrinsically increase the risk of PE by three to four folds when compared with singleton pregnancies,^[29] and this could have indirectly influenced the relationship between advanced maternal age and occurrence of PE in our study.

Population-based data from Saudi Arabia on how maternal age relates to adverse pregnancy outcomes, specifically PE, are sparse.^[2,18,20] Our research portrayed advanced maternal age (≥ 35 years) was accompanied by a higher incidence rate of PE. Our finding is in agreement with the vast body of the published literature in which there is a positive correlation between advanced maternal age and the incidence of PE.^[3,5,10,17,30] The characteristics of PE such as, mean systolic blood pressure, gestational age and etcetera were not the primary focus of the study. Similarly, the maternal and foetal outcomes of PE were not the primary goals of the present

study. Nevertheless, overall, our study, specifically, enriches the regional and international literature by providing additional data about the incidence of PE and its relationship to advanced maternal age. In addition, the findings of the present study have significant implications in clinical practice, one of which is that advanced maternal age is associated with a higher likelihood of developing PE, which should be properly counselled during antenatal visits to inform the best decision-making of childbearing.

Our study has several limitations which include the single-center experience, retrospective study design and the small sample size of patients with advanced maternal age, which may have influenced the power of statistical analysis. Additional limitations include the lack of reporting maternal and foetal outcomes of PE, which will be addressed extensively in a forthcoming research study. Moreover, other known risk factors for PE (for example, twin pregnancy, first pregnancy and family history of PE) will be investigated. Lastly, it should be noted that in our study we did not adjust (control) for other confounding variables (for example, preexisting chronic conditions, smoking, obesity, first pregnancy, history of previous PE, assisted reproductive technology and etcetera) which could have impacted the relationship between the advanced maternal age and incidence of PE.

CONCLUSIONS

In our retrospective cross-sectional study, the low prevalence of PE (4.2%) mirrored the published regional and international figures. Moreover, our research showed that advanced maternal age (≥ 35 years) constituted a substantial demographical factor implicated in developing PE. Counseling women with advanced maternal age about PE during antenatal visits should never be overlooked. More prospective, large-sized, and multi-center studies are warranted to gauge the national incidence rate of PE and its adverse pregnancy outcomes in the Saudi population in order to formulate healthcare policies.

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