Medical Science

pISSN 2321–7359; eISSN 2321–7367

Expectant versus aggressive management of severe preeclampsia at 24–34 weeks of gestation

Sarah M Ghazali[1*], **Ohoud A AlGhamdi**[2], **Nora N Sahly**[1], **Kholoud K Nagadi**[2], **Reem M Khalifah**[2], **Sedrah M Hanbazaza**[2], **Danah I Krimli**[2], **Sarah M Allaf**[2], **Renad A Turkistani**[2], **Haifa'a A Mansouri**[1]

To Cite:
Ghazali SM, AlGhamdi OA, Sahly NN, Nagadi KK, Khalifah RM, Hanbazaza SM, Krimli DI, Allaf SM, Turkistani RA, Mansouri HA. Expectant versus aggressive management of severe preeclampsia at 24–34 weeks of gestation. Medical Science 2022; 26: ms565e2659. doi: https://doi.org/10.54905/disssi/v26i130/ms565e2659

Authors' Affiliation:
[1]Department of Obstetrics and Gynecology, King Abdulaziz University, Jeddah, Saudi Arabia
[2]Medical intern, King Abdulaziz University Faculty of Medicine, Jeddah, Saudi Arabia

[*]**Corresponding Author:**
Sarah M. Ghazali
Department of Obstetrics and Gynecology, King Abdulaziz University
Email: smghazali@kau.edu.sa

Peer-Review History
Received: 06 December 2022
Reviewed & Revised: 08/December/2022 to 19/December/2022
Accepted: 22 December 2022
Published: 26 December 2022

Peer-review Method
External peer-review was done through double-blind method.

URL: https://www.discoveryjournals.org/medicalscience

ABSTRACT

Background: Preeclampsia is characterized by the onset of hypertension beyond 20 weeks of pregnancy, in addition to proteinuria and/or end-organ dysfunction, including high liver enzymes, elevated serum creatinine, thrombocytopenia, pulmonary edema, new-onset headache not responding to medications and visual disturbances. The study aimed to assess maternal and perinatal outcomes between expectant (delivery 48 h after admission) and aggressive management (delivery within 48 h) in patients with preeclampsia according to the newly defined 2020 American College of Obstetrics and Gynecology preeclampsia guideline to determine the optimal management approach.

Keywords: preeclampsia, aggressive management, preterm delivery, expectant management

1. INTRODUCTION

Preeclampsia is a serious condition and an important contributor to morbidity and mortality in both mothers and their neonates. (Ghulmiyyah & Sibai, 2012). A systematic review by Abalos et al., (2013), reported that preeclampsia is thought to complicate 4.6% of pregnancies globally. A study, conducted in the United States, showed that among 300,000 deliveries, there were approximately 1% cases of preeclampsia with severe characteristics overall (Zhang et al., 2003).

Preeclampsia is characterized by the start of new hypertension in pregnant women who was previously normotensive and who has proteinuria and/or end-organ failure after 20 weeks of gestation. Patients with preeclampsia with severe hypertension (systolic blood pressure (BP) 160 mmHg and/or diastolic blood pressure (BP) 110 mmHg) on two separate occasions, 4 hours apart, are diagnosed with preeclampsia with severe characteristics, unless antihypertensive treatment was administered, and/or signs and symptoms of

significant end-organ dysfunction, including one of the following: Thrombocytopenia less than <100 × 10^9/L, impaired liver function not due to other medical conditions defined by liver enzymes that are double the upper normal limit, severe sustained epigastric or right upper quadrant pain refractory to medication, renal failure, pulmonary edema, new-onset headache unresponsive to treatment that is not secondary to other disorders and visual disturbances (Gestational Hypertension and Preeclampsia, 2020; August & Sibai, 2022).

Diagnosis can be further categorized as early-onset (before thirty-four weeks of gestation) and late-onset (thirty-four weeks of gestation or after). Both subtypes have overlapping clinical features; however, early- and late-onset cases may differ in pathophysiology (alternatively termed placental and maternal preeclampsia, respectively) (Phipps et al., 2019). Additionally, they portray different risks and outcomes. For example, early-onset preeclampsia is associated more with fetal-growth restriction, whilst late-onset preeclampsia is associated more with maternal obesity and neonates who are large for gestational age (GA) (Rasmussen et al., 2014). Of the two subtypes, early-onset preeclampsia has a higher risk of substantial maternal and neonatal complications (Abalos et al., 2013).

Preeclampsia with severe features is associated with poor outcomes (Chen et al., 2021). Retinal detachment (or cortical blindness), disseminated intravascular coagulation, placental abruption, hypertensive encephalopathy, stroke, renal failure, liver failure, or rupture, seizures (eclampsia), myocardial infarction, cardiomyopathy and death are all serious maternal consequences. (Magee et al., 2009). Of all maternal deaths directly resulting from obstetric complications worldwide, 10–15% are associated with preeclampsia or eclampsia (Magee et al., 2009). Additionally, serious fetal complications include IUGR (more commonly with early-onset preeclampsia), neonatal respiratory distress syndrome and death (Abalos et al., 2013). The definition of preeclampsia and the criteria of severity have changed in the past few years. For example, proteinuria was a core criterion in diagnosing preeclampsia; however, it is no longer a requirement to diagnose the disease, provided evidence of end organ damage is present. The criteria of severity have been modified with the omission of greater than 5 g of proteinuria in a 24-hour urine collection, or 3+ proteinuria in the urine dipstick on two different occasions, oliguria and IUGR. The impact of these changes on maternal and perinatal outcomes has not yet been clearly demonstrated (ACOG Committee on Obstetric Practice, 2002; Gestational Hypertension and Preeclampsia, 2020).

Thus, the only definitive treatment for preterm preeclampsia with severe features remains to be established. Management includes BP control; limiting and managing symptoms, signs and complications; seizure prophylaxis; antenatal steroids; and delivery (Phipps et al., 2019). The timing of delivery after expectant management, whether immediate or delayed, remains controversial. A systematic review by Vigil-De Gracia & Ludmir, (2022) reported that increased maternal and perinatal complications are linked to conservative management of severe preeclampsia. In contrast, a Cochrane review of six randomized controlled trials (RCTs) concluded that expectant management was associated with better neonatal outcomes; however, larger-scale high-quality studies are needed (Churchill et al., 2018; Vigil-De Gracia & Ludmir, 2022).

There is a scarcity of available studies within the Saudi population regarding the most appropriate approach when dealing with preeclampsia with severe features at 24–34 weeks of gestation. Therefore, the aim of our study was to compare the maternal and perinatal outcomes between expectant (delivery 48 h after admission) and aggressive management (delivery 48 h within admission) to determine a more favorable approach.

2. MATERIALS AND METHODS

Ethics approval was obtained from the Unit of Biomedical Ethics of King Abdulaziz University Hospital (KAUH), Jeddah, Saudi Arabia. Subsequently, a retrospective cohort chart review was conducted between June 2020 October 2022 at KAUH. We included 37 cases of preeclampsia with severe features diagnosed between 24–34 weeks of gestation and divided them into two groups: Those managed aggressively by delivery within 48 h of admission and those managed expectantly and who delivered 48 h after admission.

The definition of preeclampsia with severe features was adopted from the American College of Obstetrics and Gynecology (ACOG) Practice Bulletin, Number 222 (Gestational Hypertension and Preeclampsia, 2020). We included all cases presenting with severe hypertension with a systolic BP of 160 mmHg or more, diastolic BP of 110 mmHg or more, presence or absence of proteinuria, and/or symptoms of severity. Pregnant women with hypertension >140/90 mmHg; those who did not reach the severe range; and those with or without proteinuria with one or more of elevated liver enzymes, headache, visual disturbance, mild epigastric or right upper quadrant pain and thrombocytopenia were also included. Pregnant women <24 or >34 weeks of gestation were excluded, together with women initially presenting with intrauterine fetal death, twin pregnancy, fetuses with congenital anomalies, IUGR with reversed end-diastolic flow (REDF) in the umbilical artery Doppler, abnormal fetal testing, including

abnormal fetal heart tracings, active labor, HELLP syndrome, eclampsia, or those with sustained end organ dysfunction (i.e., altered level of consciousness, pulmonary edema, stroke, posterior reversible encephalopathy syndrome and renal failure).

Our primary source of data was patient hospital electronic records, along with labor and delivery birth registration records. A pre-designed checklist was prepared to collect data on maternal age, nationality, gravidity, parity, comorbidities (chronic hypertension, gestational diabetes, hypothyroidism, previous preeclampsia, congestive heart failure, asthma, systemic lupus erythematosus), obstetric history, maternal symptoms, GA at diagnosis, BP, laboratory results (hemoglobin, hematocrit, platelets, aspartate aminotransferase (AST), alanine aminotransferase (ALT), serum creatinine, chest X-ray, brain computed tomography (CT), echocardiography, proteinuria with method of detection, obstetric ultrasonography, estimated fetal weight by ultrasound, umbilical artery Doppler, amniotic fluid volume), labor, postpartum data and maternal and fetal outcomes.

All data was analyzed using SPSS Statistics (version 21.0; IBM, Armonk, NY, USA). Continuous variables are presented as mean ± standard deviation, while categorical variables are expressed as frequencies and percentages. Continuous variables were analyzed using the t-test and data from categorical sources were analyzed using the chi-squared test. To observe the association between outcomes and different variables. Statistical significance was set at a p-value < 0.05. This study was authorized by the Institutional Review Board (IRB) of KAUH (Ref: 320-21; dated July 16, 2020). The study was conducted in accordance with the ethical standards of the responsible committee, based on the Good Clinical Practice (GCP) Guidelines. Due to the nature of the study, informed consent was not required.

3. RESULTS

Thirty-seven pregnant females diagnosed with preeclampsia and severe features that did not indicate immediate delivery were recruited. Of these, 19 (51.4%) had aggressive management with immediate delivery and 18 (48.6%) had expectant management. Maternal demographics, together with other features pertaining to obstetric and antenatal booking information, are shown in Table 1. The mean maternal age was 32.68±7.04 years and no significant difference was noted between groups. In addition, the gravidity and parity of the whole sample were 2.95±2.26 and 1.62±2, respectively and were also not significantly different between groups. Approximately a half (51.4%) of the cohort were Saudi nationals. In addition, 48.6% had medical conditions, of which 26% had chronic hypertension and 24.3% had a history of previous preeclampsia. Majority of the cohorts were un-booked during pregnancy and did not follow up with our institute, leaving 29.7% being booked during pregnancies with a mean 1.08±1.87 antenatal visits. The mean gestational age at diagnosis was 29.51±2.55, 30.37±2.03 and 28.61±2.78 weeks in the total cohort, aggressive group and expectant group, respectively, with no significant differences. The most common maternal symptom was maternal headache (83.8% of total cases), which was experienced by 78.9% and 88.9% of mothers in the aggressively managed and expectantly managed groups, respectively (Table 1). Despite the small sample size, women with severe preeclampsia presenting with visual disturbances were significantly more likely to have been treated more aggressively than expected ($P < 0.05$).

Table 1 Comparison between aggressive and expectant management according to maternal demographics, obstetric data, antenatal booking status, number of visits, maternal symptoms, blood pressure and gestational age at diagnosis

Variable	Total No.(%) N=37	Start of labor		*P*-value
		Aggressive management (No.:19) No. (%)	Expectant management (No.:18) No. (%)	
Maternal age	32.68 ± 7.04	31.32 ± 6.99	34.11 ± 6.99	0.271
Gravidity	2.95 ± 2.26	2.79 ± 2.41	3.11 ± 2.13	0.425
Parity	1.62 ± 2	1.58 ± 2.29	1.67 ± 1.71	0.538
Nationality Saudi Non-Saudi	 19 (51.4) 18 (48.6)	 8 (42.1) 11 (57.9)	 11 (61.1) 7 (38.9))	0.248
History of medical disease No Yes If yes, what disease?	 19 (51.4) 18 (48.6)	 10 (52.6) 9 (47.4)	 9 (50) 9 (50)	0.873

Chronic hypertension	9 (24.3)	3 (15.8)	6 (33.3)	0.214
Gestational diabetes mellitus	5 (13.5)	1 (5.3)	4 (22.2)	0.132
Hypothyroidism	3 (8.1)	2 (10.5)	1 (5.6)	0.58
Previous preeclampsia	9 (24.3)	4 (21.1)	5 (27.8)	0.634
Cardiac heart failure	1 (2.7)	1 (5.3)	0 (0.0)	0.324
Asthma	1 (2.7)	0 (0.0)	1 (5.6)	0.298
Systemic lupus erythematosus	1 (2.7)	0 (0.0)	1 (5.6)	0.298
Booking status, n (%)				
Booked	11 (29.7)	4 (21.1)	7 (38.9)	0.235
Unbooked	26 (70.3)	15 (78.9)	11 (61.1)	
Number of miscarriages	0.32 ± 0.62	0.21± 0.53	0.47± 0.71	0.33
Number of antenatal visits	1.08 ± 1.87	0.53 ± 1.02	1.67 ± 2.37	0.21
Maternal symptoms, n (%)				
Headache	31 (83.8)	15 (78.9)	16 (88.9)	0.412
Lower limb edema	3 (8.1)	3 (15.8)	0 (0.0)	0.079
Epigastric pain	6 (16.2)	2 (10.5)	4 (22.2)	0.335
Visual disturbances	10 (27)	8 (42.1)	2 (11.1)	0.034
Chest pain	3 (8.1)	1 (5.3)	2 (11.1)	0.515
Abdominal pain	2 (5.4)	1 (5.3)	1 (5.6)	0.969
Generalized edema	1 (2.7)	0 (0.0)	1 (5.6)	0.289
Right upper quadrant pain	1 (2.7)	0 (0.0)	1 (5.6)	0.298
Vaginal spotting	1 (2.7)	0 (0.0)	1 (5.6)	0.298
Nausea, vomiting, eclampsia	1 (2.7)	0 (0.0)	1 (5.6)	0.298
Highest systolic blood pressure (mmHg)	177.89 ± 20.4	176.21 ± 19.97	179.67 ± 21.27	0.805
Highest diastolic blood pressure (mmHg)	105.38 ± 11.73	104.16 ± 11.76	106.67 ± 11.89	0.73
Gestational age at diagnosis (weeks)	29.51 ± 2.55	30.37 ± 2.03	28.61 ± 2.78	0.057

* Independent sample t-test; ** Mann–Whitney U test

Upon presentation, the mean systolic and diastolic BP of the patients were 177.89±20.4 mmHg and 105.38±11.73 mmHg, respectively, with no significant difference between groups (Table 1). Most women with severe preeclampsia did not have proteinuria and when present (29.7%), it was mostly detected in urine using clean-catch by dipstick and was significant (≥+2) in approximately 70.3% of cases. Laboratory and radiological data were generally comparable between groups (Table 2). Most participants were anemic, 70.3% had a low hemoglobin level, 64.9% had a low hematocrit level and 10.8% had a low platelet level. In addition, about a quarter of the women had disturbed liver enzymes with high levels of AST (27%) and ALT (21.8%) and only 2.7% showed abnormally elevated serum creatinine. Only 18.8%, 2.7% and 2.7% of the participants underwent chest X-ray, brain CT and echocardiography, respectively. Over half (54.1%) of booked women who had a detailed obstetric ultrasound were found to have IUGR. Most (70.3%) patients showed only increased resistance on the umbilical artery Doppler, while 2.7% and 13.5% had absent end-diastolic flow (AEDF) or REDF, respectively. Regarding REDF, all cases developed later in the expectantly managed group. Abnormal Dopplers were noted in very-early-onset IUGR cases, all of which were at <28 weeks of gestation when surveillance was started. Only 18.9% had an abnormal amniotic fluid volume.

Table 2 Comparison between aggressive and expectant management according to laboratory results and investigations

Variable	Total No. (%) (N=37)	Start of labor		*P*-value
		Aggressive management (No.:19) No. (%)	Expectant management (No.:18) No. (%)	
Hemoglobin status, n (%)				
Normal	10 (27)	3 (15.8)	7 (38.9)	
Low	26 (70.3)	16 (84.2)	10 (55.6)	0.138
High	1 (2.7)	0 (0.0)	1 (5.6)	

Hematocrit status, n (%)				
Normal	13 (35.1)	5 (26.3)	8 (44.4)	0.248
Low	24 (64.9)	14 (73.7)	10 (55.6)	
Platelet status, n (%)				
Normal	33 (89.2)	17 (89.5)	16 (88.9)	0.954
Low	4 (10.8)	2 (10.5)	2 (11.1)	
AST status, n (%)				
Normal	22 (59.5)	12 (63.2)	10 (55.6)	
Low	5 (13.5)	3 (15.8)	2 (11.1)	0.685
High	10 (27)	4 (21.1)	6 (33.3)	
ALT status, n (%)				
Normal	25 (67.6)	14 (73.7)	11)61.1)	
Low	4 (10.8)	3 (15.8)	1 (5.6)	0.189
High	8 (21.8)	2 (10.5)	6 (33.3)	
Serum creatinine status, n (%)				
Normal	20 (54.1)	9 (47.4)	11 (61.1)	
Low	16 (43.2)	9 (47.4)	7 (38.9)	0.491
High	1 (2.7)	1 (5.3)	0 (0.0)	
Chest X-ray, n (%)				
Done	7 (18.9)	4 (21.1)	3 (16.7)	0.734
Not done	30 (81.1)	15 (78.9)	15 (83.3)	
Brain CT, n (%)				
Done	1 (2.7)	1 (5.3)	0 (0.0)	0.324
Not done	36 (97.3)	18 (94.7)	18 (100)	
Echocardiography, n (%)				
Done	1 (2.7)	0 (0.0)	1 (5.6)	0.298
Not done	36 (97.3)	19 (100)	17 (94.4)	
Proteinuria, n (%)				
No	26 (70.3)	12 (63.2)	14 (77.8)	0.331
Yes	11 (29.7)	7 (36.8)	4 (22.2)	
Method of detecting proteinuria, n (%)				
None	10 (27)	7 (36.8)	3 (16.7)	
Dipstick (≥ +2)	26 (70.3)	11 (57.9)	15 (83.3)	0.203
24-h urine protein ≥300 mg	1 (2.7)	1 (5.3)	0 (0.0)	
Obstetric ultrasound, n (%)				
No	35 (94.6)	17 (89.5)	18 (100)	0.157
Yes	2 (5.4)	2 (10.5)	0 (0.0)	
EFW by ultrasound, n (%)				
Normal	15 (40.4)	10 (52.6)	5 (27.8)	
IUGR	20 (54.1)	7 (36.8)	13 (72.2)	0.066
NA	2 (5.4)	2 (10.5)	0 (0.0)	
Umbilical artery Dopplers, n (%)				
Normal	5 (13.5)	2 (10.5)	3 (16.7)	
Increased resistance	26 (70.3)	17 (89.5)	9 (50)	
Absent EDF	1 (2.7)	0 (0.0)	1 (5.6)	0.034
Reversed EDF	5 (13.5)	0 (0.0)	5 (27.8)	
Amniotic fluid volume, n (%)				
Normal	30 (81.1)	18 (94.7)	12 (66.7)	0.029
Abnormal	7 (18.9)	1 (5.3)	6 (33.3)	

AST, aspartate aminotransferase; ALT, alanine aminotransferase; CT, computed tomography; EFW, estimated fetal weight; IUGR, intrauterine growth restriction; NA, not applicable; EDF, end-diastolic flow

Almost all women (91.9%; $P < 0.05$) delivered by cesarean section due to severe preeclampsia, as decided by the consultant taking care of the case, rather than non-reassurance of fetal status. The mean duration of the total hospital stay for the mother was 6.38±3.98 days. Only 5 of the 37 women had maternal complications, such as antepartum hemorrhage, upper limb numbness and weakness, or postpartum bleeding. Women who underwent aggressive management had a significantly shorter mean duration of hospital stay (4.58±1.86 days vs. 8.28±4.75 days; $P < 0.05$) (Table 3 and Figure 1). There were no maternal deaths or intensive care unit (ICU) admissions.

Table 3 Comparison between expectant versus aggressive management according to labor and postpartum data

Variable	Total No. (%)	Start of labor		*P*-value
		Aggressive management (No.:19) No. (%)	Expectant management (No.:18) No. (%)	
Mode of delivery, n (%)				
Spontaneous vaginal delivery	3 (8.1)	0 (0.0)	3 (16.7)	
Cesarean section	34 (91.9)	19 (100)	15 (83.3)	0.063
Reason for cesarean section (n=34)				
Severe preeclampsia physician decision, n (%)	28 (82.4)	13 (68.4)	15 (100)	0.016
Non-assuring fetal status, n (%)	6 (17.6)	6 (31.6)	0 (0.0)	
Indication for delivery, n (%)				
Severe IUGR	1 (2.7)	0 (0.0)	1 (5.6)	
Decelerations	5 (13.5)	4 (21.1)	1 (5.6)	
Fetal distress	1 (2.7)	0 (0.0)	1 (5.6)	
Severe headache	1 (2.7)	1 (5.3)	0 (0.0)	0.052
Severe preeclampsia	5 (5.4)	5 (26.3)	0 (0.0)	
Uncontrolled hypertension	2 (5.4)	0 (0.0)	2 (11.1)	
Duration of hospital stay (days)	6.38 ± 3.98	4.58 ± 1.86	8.28 ± 4.75	0.004
Maternal complications, n (%)				
No	32 (86.5)	17 (89.5)	15 (83.3)	
Yes	5 (13.5)	2 (10.5)	3 (16.7)	0.585
If yes, what complication? (n=5)				
Antepartum hemorrhage (abruption)	1 (20)	0 (0.0)	1 (5.6)	
First-degree perineal laceration	1 (20)	0 (0.0)	1 (5.6)	
Headache, blurred vision, right upper limb numbness and weakness	1 (20)	1 (5.3)	0 (0.0)	0.404
HELLP syndrome	1 (20)	0 (0.0)	1 (5.6)	
PV bleeding with clots - LL edema	1 (20)	1 (5.3)	0 (0.0)	

* Mann–Whitney U test; ** independent sample t-test. IUGR, intrauterine growth restriction; PV, (per vaginal bleeding); LL, (lower limb)

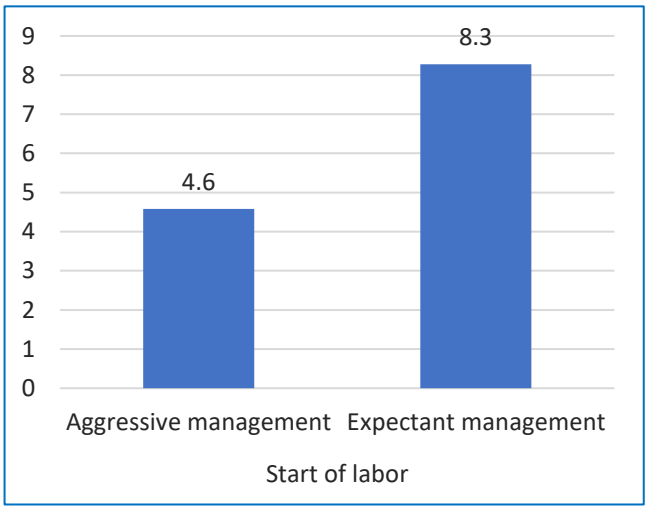

Figure 1 Duration of hospital stay (days)

The mean GA at delivery in the entire sample was 30.24±2.24 weeks, 30.68±1.82 weeks in the aggressive group and 28.78±2.57 in the expectant group, with no significant difference. At least one dose of antenatal steroids was administered to all patients. The mean birth weight of babies upon delivery was 1.16±0.49 kg with no difference between groups (1.21±0.47 kg in the aggressive group and 1.11±0.51 kg in the expectant group). The mean Apgar score was 5.11±3.16 at 1 min and 6.86±3.39 at 5 min with no significant difference between groups. Most neonates (94.6%) were admitted to the neonatal ICU, 64.9% had respiratory distress, and 89.2% were discharged alive (Table 4).

Table 4 Comparison between expectant versus aggressive management according to perinatal outcome, gestational age at delivery, and pregnancy outcome

Variable	Total No. (%)	Start of labor		*P*-value
		Aggressive management (No.:19) No. (%)	Expectant management (No.:18) No. (%)	
Gestational age at delivery (days)	30.24 ± 2.24	30.68 ± 1.82	28.78 ± 2.57	0.358
Apgar score at 1 min	5.11 ± 3.16	6.44± 1.65	6.29 ± 2.71	0.684
Apgar score at 5 min	6.86 ± 3.39	8.33 ± 1.02	7.71 ± 2.61	0.832
Birthweight (kg)	1.16 ± 0.49	1.21 ± 0.47	1.11 ± 0.51	0.291
Prenatal outcome, n (%) Discharged alive Early neonatal death Late neonatal death	 33 (89.2) 2 (5.4) 2 (5.4)	 19 (100) 0 (0.0) 0 (0.0)	 14 (77.8) 2 (11.1) 2 (111.)	0.094
Neonatal outcome, n (%) Free Respiratory distress Neonatal jaundice	 11 (29.7) 24 (64.9) 2 (5.4)	 5 (26.3) 14 (73.7) 0 (0.0)	 6 (35.3) 10 (58.8) 1 (5.9)	0.438
NICU admission, n (%) Yes No	 35 (94.6) 2 (5.4)	 19 (100) 0 (0.0)	 16 (88.9) 2 (11.1)	0.135
Duration of NICU admission (days)	42.8 ± 45.34	42.46 ± 50.17	43.19 ± 40.47	0.883

* Mann–Whitney U test; ** independent sample t-test. NICU, neonatal intensive care unit

4. DISCUSSION

Our study showed that maternal and neonatal outcomes in preterm preeclampsia with severe features in our population, using the new ACOG guidelines, did not differ whether expectantly managed with delayed delivery or aggressively managed by early

delivery. Expectant management was only associated with extended hospital stays, resource and economic burden. This finding is consistent with those of a randomized controlled trial conducted in Latin America, in which 267 women with preterm preeclampsia and severe features at 28–33 weeks of gestation underwent prompt delivery or expectant management. They found no neonatal benefit in those managed expectantly (Vigil-De Gracia et al., 2013). A systematic review of observational trials by Vigil-De Gracia & Ludmir, (2022) also concluded that expectant management of preterm preeclampsia without HELLP syndrome or IUGR when prolonging the pregnancy by 2 days or more was associated with more maternal complications or perinatal deaths. In contrast, a Cochrane review of six randomized clinical trials including 748 women concluded that expectant management of severe preterm preeclampsia was associated with less neonatal morbidity (Churchill et al., 2018); however, only two studies in that review with low-quality evidence had data regarding maternal complications and so this remains uncertain. Large-scale randomized control trials are needed to establish the best management approach for preterm preeclampsia with newly defined severe features.

In our study, 91.9% of patients underwent cesarean section, with 100% in the aggressive group and 83.3% in the expectant group. This is comparable to what was reported by Vigil-De Gracia et al., (2013), in which 88.7% of early delivery cases and 94.7% of expectantly managed cases were delivered via cesarean section. In a systematic review comparing the outcomes of conservative management of preterm preeclampsia associated with severe features between RCTs and observational trials, it was found that 87% of patients happened to be delivered by cesarean section in the RCTs compared to 55% in the observational trials. Mashiloane & Moodley, (2002) showed that elective cesarean sections in patients with preterm preeclampsia were associated with improved perinatal outcomes compared with those who delivered vaginally or required emergency cesarean section for failed induction of labor (IOL).

Another study showed that IOL in patients with preeclampsia had a higher failure rate than in those without (Xenakis et al., 1997). On the contrary, they showed that successful IOL with vaginal delivery in patients with early severe preeclampsia was achieved in 53.5% of cases without worsening neonatal outcomes. They also demonstrated a reduced induction success rate with decreasing GA at delivery. Their success was 6.7% between 24–28 weeks, 47.5% between 28–32 weeks and 68.8% between 32–34 gestational weeks (Alanis et al., 2008). Coviello et al., (2019) also showed that half of the women with preterm preeclampsia delivered vaginally after IOL and the success rate increased with increasing GA. The rates of maternal and perinatal complications did not differ between the IOL and elective cesarean groups, but a higher maternal morbidity was reported if the IOL failed. Similar findings were also observed by Blackwell et al., (2001), with an overall success rate of IOL in preterm preeclampsia of 46% without an increase in neonatal morbidity and higher failure rates with IOL below 28 weeks of gestation. There was a high rate of respiratory distress syndrome in the neonates in our study despite antenatal steroids; this could be the additive effect of cesarean section on top of prematurity. A meta-analysis by Li et al., (2019), concluded that cesarean section increased the risk of respiratory distress syndrome in neonates. In view of these studies, careful selection of patients for IOL appears to be the most effective method.

IUGR complicated 54.1% of our cases, with a tendency for more cases in the expectant management group (72.2% vs. 36.8%; $P = 0.066$). Increased resistance in the umbilical artery Doppler was found in 70.3% of our cohort and AEDF and REDF occurred later in very-preterm (<28 weeks) patients in the expectant management group. This may explain the absence of a benefit of expectant management in our study. IUGR was an exclusion criterion in an RCT by Sibai et al., (1994) and better neonatal outcomes, including fewer neonatal ICU admissions and less respiratory distress syndrome, were seen in preterm women with preeclampsia managed expectantly versus aggressively. Shear et al., (2005) demonstrated in their retrospective cohort of preterm severe preeclampsia that the main predictor of poor neonatal outcomes was delivery at GA < 30 weeks, irrespective of growth restriction status. They strongly recommended expectant management of fetuses. Haddad et al., (2007) showed that expectant management of severe preterm preeclampsia with severe IUGR at 23–33 weeks has a higher risk of intrauterine fetal deaths, but there was no difference in neonatal morbidity or maternal complications compared to patients with non-severe IUGR. The optimal timing of delivery of growth-restricted fetuses in the setting of preterm preeclampsia presenting with severe features warrants further investigation.

Our study incorporated both maternal and fetal complications and outcomes in detail. This study highlights how changes in the definition and criteria of severe preeclampsia may impact its management course and outcome. Moreover, when focusing on maternal symptoms, our study indicated that certain clinical features, namely visual disturbances, may require more prompt management than others, thus leading to more research questions regarding disease risk stratification and delivery strategies, especially with co-occurring IUGR. In addition, it is unclear whether there are genetically or geographically unique preeclampsia disposition spectra. There will hopefully be a more detailed explanation and protocol for such an enigmatic and highly morbid disorder.

The limitations of our study include the need for a larger sample size, to be conducted as a high-quality RCT with an intention to treat and subgroup analysis to determine risk groups along with the optimal strategy in managing women with severe preeclampsia safely and with the best maternal and fetal outcomes.

5. CONCLUSION

In our study population, no significant difference was found in the maternal or neonatal outcomes of patients with preterm preeclampsia with severe features, whether aggressively or expectantly managed. The impact of a high rate of IUGR on this finding is unclear. Further studies using the new definition of severe features and the impact and timing of delivery of growth-restricted fetuses in this setting are warranted.

Authors' contributions

Sarah M Ghazali (supervised the study, participated in reviewing the data, writing and reviewing the manuscript)
Ohoud A AlGhamdi, Kholoud K Nagadi, Reem M Khalifah, Sedrah M Hanbazaza, Danah I Krimli, Renad A Turkistani and Sarah M Allaf (participated in the literature review, data collection, data analysis, manuscript original draft writing)
Ohoud A AlGhamdi and Kholoud K Nagadi (editing and reviewing the final manuscript)
Nora N Sahly (participated in the data analysis, reviewed the results and final manuscript)
Haifa'a A Mansouri (conceptualized the study)
All authors have read and approved the manuscript's final version.

Ethical approval

The study was approved by the Medical Ethics Committee of King Abdulaziz University (code: 320-21).

Acknowledgment

We would like to thank all patients whose data constituted our study sample.

Informed consent

Not applicable.

Funding

This study has not received any external funding.

Conflict of interest

The authors declare that there is no conflict of interests.

Data and materials availability

All data sets collected during this study are available upon reasonable request from the corresponding author.

REFERENCES AND NOTES

1. Abalos E, Cuesta C, Grosso AL, Chou D, Say L. Global and regional estimates of preeclampsia and eclampsia: A systematic review. Eur J Obstet Gynecol Reprod Biol 2013; 170:1-7. doi: 10.1016/j.ejogrb.2013.05.005
2. ACOG Committee on Obstetric Practice. ACOG practice bulletin. Diagnosis and management of preeclampsia and eclampsia. Number 33, January 2002. American College of Obstetricians and Gynecologists. Int J Gynaecol Obstet 2002; 77:67-75.
3. Alanis MC, Robinson CJ, Hulsey TC, Ebeling M, Johnson DD. Early-onset severe preeclampsia: Induction of labor vs elective cesarean delivery and neonatal outcomes. Am J Obstet Gynecol 2008; 199:262.e1-6. doi: 10.1016/j.ajog.2008.06.076
4. August P, Sibai BM. Preeclampsia: Clinical features and diagnosis. 2022. Available from: https://www.uptodate.com/contents/preeclampsia-clinical-features-and-diagnosis
5. Blackwell SC, Redman ME, Tomlinson M, Landwehr JB Jr, Tuynman M, Gonik B, Sorokin Y, Cotton DB. Labor induction for the preterm severe pre-eclamptic patient: Is it worth the effort? J Matern Fetal Med 2001; 10:305-11. doi: 10.1080/714904348
6. Chen Z, Zhang W, Wu M, Huang H, Zou L, Luo Q. Pathogenic mechanisms of preeclampsia with severe

features implied by the plasma exosomal mirna profile. Bioengineered 2021; 12:9140-9. doi: 10.1080/21655979.2021.1993717

7. Churchill D, Duley L, Thornton JG, Moussa M, Ali HS, Walker KF. Interventionist versus expectant care for severe pre-eclampsia between 24 and 34 weeks' gestation. Cochrane Database Syst Rev 2018; 10:CD003106. doi: 10.1002/14651858.CD003106.pub3
8. Coviello EM, Iqbal SN, Grantz KL, Huang CC, Landy HJ, Reddy UM. Early preterm preeclampsia outcomes by intended mode of delivery. Am J Obstet Gynecol 2019; 220:100.e1-9. doi: 10.1016/j.ajog.2018.09.027
9. Gestational Hypertension and Preeclampsia: ACOG Practice Bulletin, Number 222. Obstet Gynecol 2020; 135:e237-60. doi: 10.1097/AOG.0000000000003891
10. Ghulmiyyah L, Sibai B. Maternal mortality from preeclampsia/eclampsia. Semin Perinatol 2012; 36:56-9. doi: 10.1053/j.semperi.2011.09.011
11. Haddad B, Kayem G, Deis S, Sibai BM. Are perinatal and maternal outcomes different during expectant management of severe preeclampsia in the presence of intrauterine growth restriction? Am J Obstet Gynecol 2007; 196:237.e1-5. doi: 10.1016/j.ajog.2006.10.905
12. Li Y, Zhang C, Zhang D. Cesarean section and the risk of neonatal respiratory distress syndrome: A meta-analysis. Arch Gynecol Obstet 2019; 300:503-17. doi: 10.1007/s00404-019-05208-7
13. Magee LA, Yong PJ, Espinosa V, Cote AM, Chen I, Von Dadelszen P. Expectant management of severe preeclampsia remote from term: A structured systematic review. Hypertens Pregnancy 2009; 28:312-47. doi: 10.1080/10641950802601252
14. Mashiloane CD, Moodley J. Induction or caesarean section for preterm pre-eclampsia? J Obstet Gynaecol 2002; 22:353-6. doi: 10.1080/01443610220141245
15. Phipps EA, Thadhani R, Benzing T, Karumanchi SA. Pre-eclampsia: Pathogenesis, novel diagnostics and therapies. Nat Rev Nephrol 2019; 15:275-89. doi: 10.1038/s41581-019-0119-6 Erratum in: Nat Rev Nephrol 2019; 15:386.
16. Rasmussen S, Irgens LM, Espinoza J. Maternal obesity and excess of fetal growth in pre-eclampsia. Int J Gynaecol Obstet 2014; 121:1351-7. doi: 10.1111/1471-0528.12677
17. Shear RM, Rinfret D, Leduc L. Should we offer expectant management in cases of severe preterm preeclampsia with fetal growth restriction? Am J Obstet Gynecol 2005; 192:1119-25. doi: 10.1016/j.ajog.2004.10.621
18. Sibai BM, Mercer BM, Schiff E, Friedman SA. Aggressive versus expectant management of severe preeclampsia at 28 to 32 weeks' gestation: A randomized controlled trial. Am J Obstet Gynecol 1994; 171:818-22. doi: 10.1016/0002-9378(94)90104-x
19. Vigil-De Gracia P, Ludmir J. Conservative management of early-onset severe preeclampsia: Comparison between randomized and observational studies a systematic review. J Matern Fetal Neonatal Med 2022; 35:3182-9. doi: 10.1080/14767058.2020.1814249
20. Vigil-De Gracia P, Tejada OR, Miñaca AC, Tellez G, Chon VY, Herrarte E, Villar A, Ludmir J. Expectant management of severe preeclampsia remote from term: The MEXPRE Latin Study, a randomized, multicenter clinical trial. Am J Obstet Gynecol 2013; 209:425.e1-8. doi: 10.1016/j.ajog.2013.08.016
21. Xenakis EM, Piper JM, Field N, Conway D, Langer O. Preeclampsia: Is induction of labor more successful? Obstet Gynecol 1997; 89:600-3. doi: 10.1016/S0029-7844(97)00043-4
22. Zhang J, Meikle S, Trumble A. Severe maternal morbidity associated with hypertensive disorders in pregnancy in the United States. Hypertens Pregnancy 2003; 22:203-12. doi: 10.1081/PRG-120021066