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Review

Uterine hemangioma in pregnancy: A case report and review of the literature

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ABSTRACT

Introduction: Uterine hemangioma is a rare benign vascular tumor which can cause bleeding problems in various age groups. Current knowledge on this rare condition in pregnancy is limited. We report on a recent case of uterine hemangioma in a pregnancy that was already diagnosed during her first trimester. We also provide a literature review to summarize the characteristics and outcomes of uterine hemangioma cases in pregnant women.

Material and methods: A systematic search was done of all published literature up to February 2021 using PubMed and Scopus databases. The selection process was registered using the online tool Rayyan QCRI. All data was described in a narrative format. The protocol was prospectively registered on PROSPERO (CRD42021237519).

Results: Fifteen case reports were included. In most cases, the diagnosis was established by antenatal ultrasound. More than half of the women developed a postpartum hemorrhage, necessitating a hysterectomy for bleeding control in half of the cases, although the risk for both seemed lower in those women in whom the hemangioma was diagnosed before delivery. One case of maternal mortality and two cases of fetal death were reported. There was one case of neonatal respiratory morbidity, although the neonatal data were not routinely reported upon.

Conclusion: Current knowledge on uterine hemangioma in pregnancy is limited, but it seems to hold substantial risks for both pregnant women and their unborn child. We recommend routine screening for this condition at the standard mid-trimester anomaly scan. Pregnant women with uterine hemangioma should ideally be cared for in centers of expertise. An international registry will help to build a better understanding of this rare pathology.

Introduction

Hemangiomas are benign vascular tumors that originate from either endothelial cells lining the vessels or pericytes that are found outside the vascular wall [1]. They consist of multiple anastomosing vessels lined by a single layer of endothelium. Hemangiomas are named 'capillary' when they are composed of small size capillary vessels, and 'cavernous' if they consist of large anastomosing vascular spaces ('caverns') [1–5]. They are commonly found in the head and neck region and only rarely occur in the uterus, the exact incidence of uterine hemangioma is unknown [6]. Uterine hemangiomas can involve all levels of the uterine wall, most notably the myometrium [7]. The lesion has been described in various age groups and is known to have many heterogenous clinical presentations, commonly reported in the context of obstetric complications [1–3].

Current literature on uterine hemangioma in pregnancy mainly consists of case reports. The hormonal and physical changes of pregnancy have been proposed to affect these pre-existing lesions. The most reported complication is peripartum hemorrhage which can be life-threatening [2,8]. Diagnosis is often made on hysterectomy specimens or more recently through antepartum imaging, by ultrasound (US) and/or magnetic resonance imaging (MRI) [9]. The typical findings being substantially thickened myometrium due to diffuse venous plexuses that contain low flow rates.

Herein we present a recent case in our tertiary care center followed by a narrative review of all published uterine hemangioma cases in pregnant women.

Abbreviations: MRI, magnetic resonance imaging; US, ultrasound

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Material and methods

The protocol for this literature review was prospectively registered on The International Prospective Register of Systematic Reviews (PROSPERO, registration number CRD42021237519). We reported it according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [10].

Data sources

We searched the electronic databases PubMed and Scopus from their inception until 21 February 2021 using the following search terms: "((hemangioma) OR (cavernous) OR (vascular malformation)) AND (pregnancy) AND (uterus)". We also screened the reference list of all retrieved articles to identify additional eligible articles not captured by our electronic search, thereby identifying 2 additional case reports.

Main outcome measures

The primary outcomes were maternal and neonatal (until discharge) mortality and morbidity. Secondary outcomes were the occurrence of pregnancy complications, preterm delivery rate, perinatal blood loss, perinatal hysterectomy incidence and neonatal ICU-admission.

Eligibility criteria

We included case reports, case series, randomized studies, and case control studies. All articles of other types (systematic reviews, narrative review articles and studies published only as abstracts) were excluded. Non-English articles were also excluded, except for those with an English abstract that already provided the primary outcomes.

Study participants were pregnant women with a hemangioma of the uterine corpus, diagnosed either before, during or directly after pregnancy. Articles reporting on non-pregnant women with uterine hemangioma that provided information on their obstetrical history were also included.

Data collection and analysis

The online tool Rayyan QCRI was used for registration of the selection process [11]. Duplicate articles were automatically excluded. Two assessors (EB and JvdM) independently screened all titles and abstracts. Eligible articles were retained for full-text reading. Uncertainties at each stage were discussed and resolved by consensus with a low threshold for inclusion.

One reviewer (EB) extracted all data on pregnancy course and complications occurring during delivery and the postpartum period, which was thereafter verified by the second reviewer (JvdM). Uncertainties at each stage were again discussed and resolved by consensus. All data were described in a narrative format.

Case report

A 30-year-old nulliparous patient was referred to our center, University Hospitals Leuven, for a suspicion of a molar pregnancy at the first ultrasound check-up with her gynecologist. She had an unremarkable medical and familial history. On initial ultrasound examination, an intrauterine pregnancy with crown-rump length (CRL) corresponding to a gestational age of 8 weeks 4 days was seen. The trophoblast appeared normal, but the myometrium was overall diffusely thickened due to venous plexuses that contained low flow rates (Fig. 1). The presumptive diagnosis of a uterine hemangioma was confirmed on MRI at 10 weeks of gestation that demonstrated marked T2-hyperintens, T1-hypointens and non-diffusion restrictive enlargement of the entire myometrium enclosing multiple vessels (Fig. 2).

The course of the pregnancy was rather uneventful, except for a minor bleeding episode at 13 weeks of pregnancy and a short admission at 28 weeks due to a single episode of nonspecific lower abdominal pain. The sonographic appearance of the myometrium remained unchanged during pregnancy (Fig. 3). The patient was hospitalised from her 36th week of pregnancy onwards for observation to address the increased intra- and postpartum bleeding risk.

An elective delivery at 38 weeks and 5 days was planned with a senior pelvic surgeon and interventional radiology team on standby. Labor was induced by means of prostaglandin E2 administration and subsequent artificial rupture of the membranes. This was followed by oxytocin labor augmentation and a spontaneous vaginal delivery of a healthy son weighing 2835 gs. Apgar scores were 9/10/10 and umbilical artery pH was 7.29. Intravenous carbetocin 100 μg and tranexamic acid 1 g were administered immediately, but within minutes a primary postpartum hemorrhage occurred with the placenta still in-utero. Sulprostone 500 μg perfusion was initiated, and a manual removal of the placenta was done. Additionally, a gentle curettage was performed to remove some retained membranes after which the uterus atony resolved, and the bleeding ceased. The total blood loss was estimated to be 1200 mL. Both the mother and newborn had an unremarkable postpartum course. Prophylactic postpartum low-molecular-weight heparin was continued for 6 weeks. After 3 months the myometrial hemangioma was markedly regressed on ultrasound. A whole-body MRI performed 8 months after delivery additionally noted a small 11 mm hemangioma in the liver segment 7.

Written consent was obtained from the patient whose case is presented above.

Results

Of the initial 476 identified articles, 23 full text articles were assessed for eligibility. Eventually, 15 case reports were included in this review (Fig. A1). The baseline patient characteristics, clinical presentation, and mode of diagnosis in the 15 pregnancies described in these publications are given in Table 1. An overview of the pregnancy course and the maternal and neonatal outcomes is provided in Table 2.

Of the 15 pregnancies, two (2/15, 13.3%) resulted in a stillbirth possibly due to the uterine hemangioma. The first one occurred at 28 weeks after massive thrombosis of the uterine and placental vessels, the latter following acute rupture of the uterine hemangioma at 36 weeks. Another two pregnancies were delivered preterm (2/15, 13.3%). One patient delivered at 35 weeks after preterm prelabour rupture of the membranes (PPROM) at 26 weeks, and a second patient had a cesarean section at 30 weeks due to progressive abdominal discomfort and the assumed bleeding risk of the hemangioma. Forty percent of women (6/15, 40.0%) went into labor spontaneously, which resulted into a vaginal delivery in four cases. Most women were delivered by cesarean section (10/15, 66.7%), of which seven (7/10, 70%) were unplanned/in an emergency setting. The postpartum period was complicated by a hemorrhage in eight women (8/15, 53.3%), which necessitated a hysterectomy in four cases (4/8, 50%). Two women developed progressive hypovolemic shock (2/8, 25%). Of those for whom data was provided (5/8, 62.5%), all had an estimated blood loss of $\geq$ 1000 mL. Furthermore, another two women developed a pulmonary embolism in the postpartum period, ultimately fatal in one of them. Perinatal outcomes were mentioned in only six reports (6/15, 40%). Only half of these cases (3/6, 50%) had an uneventful outcome. One case of respiratory problems due to preterm birth at 30 weeks was described beyond the two stillbirths mentioned above.

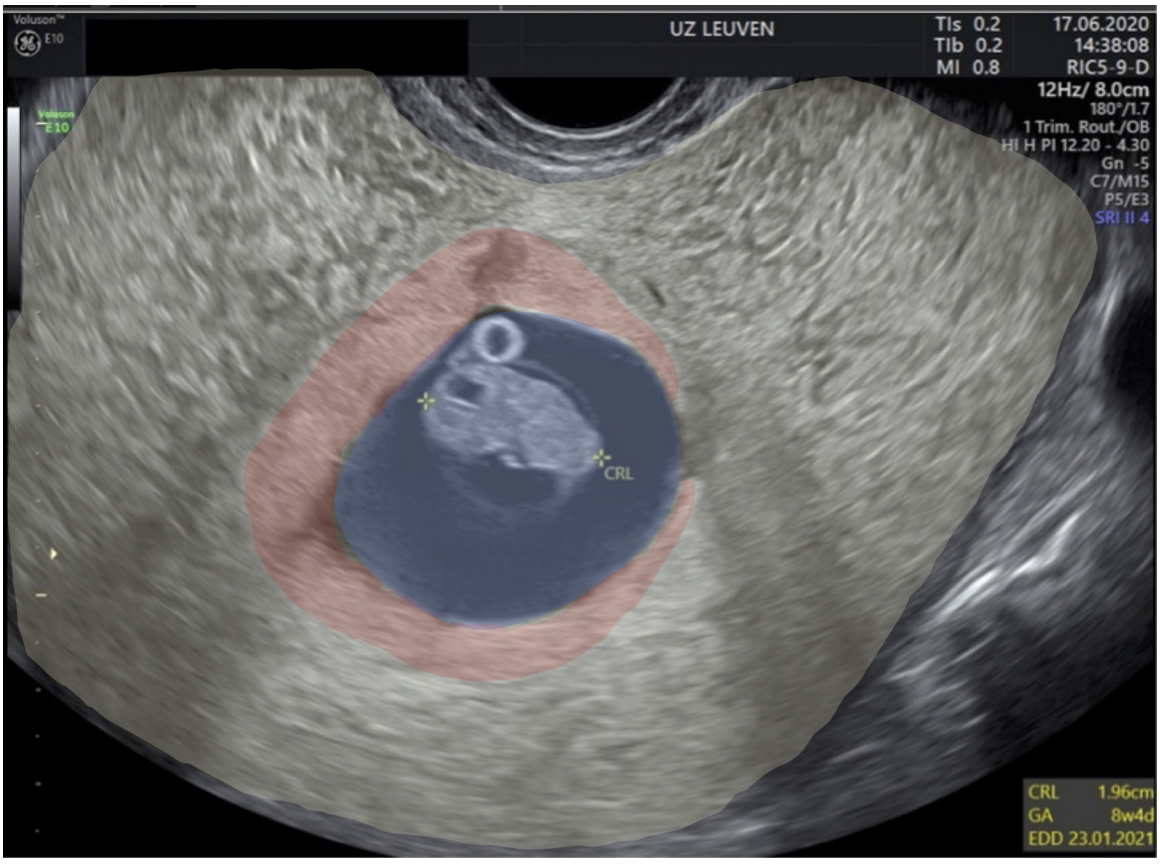

Fig. 1. Transvaginal ultrasound image upon referral of the patient at 8 weeks and 4 days showing the gestational sac (blue), the developing placenta (red) and the diffusely thickened myometrium due to venous plexuses (yellow). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.).

The hemangioma was diagnosed before delivery in the majority of cases (10/15, 66.7%), generally during the second trimester of pregnancy. Most often, symptoms such as abdominal discomfort, dyspnea, or vaginal bleeding and/or the finding of an enlarged uterus led to a work-up. Four patients were referred for abnormal ultrasound findings, which in all but one case were based upon the suspicion of a partial mole. The antenatal diagnosis was generally based on ultrasound findings, MRI was used to confirm the hemangioma in only one patient.

Half of the patients (5/10, 50%) with an established diagnosis of hemangioma before delivery had a non-planned cesarean section. In two of these patients (2/5, 40%), this was for reasons related to the hemangioma: one patient had a cesarean section for fetal death at 28 weeks and another patient was delivered at 30 weeks due to progressive abdominal discomfort as mentioned earlier. Five of the 10 antenatal diagnosed patients (5/10, 50%) developed a postpartum hemorrhage, which necessitated a hysterectomy in only one of them. Among the patients with an antenatal diagnosis of a uterine

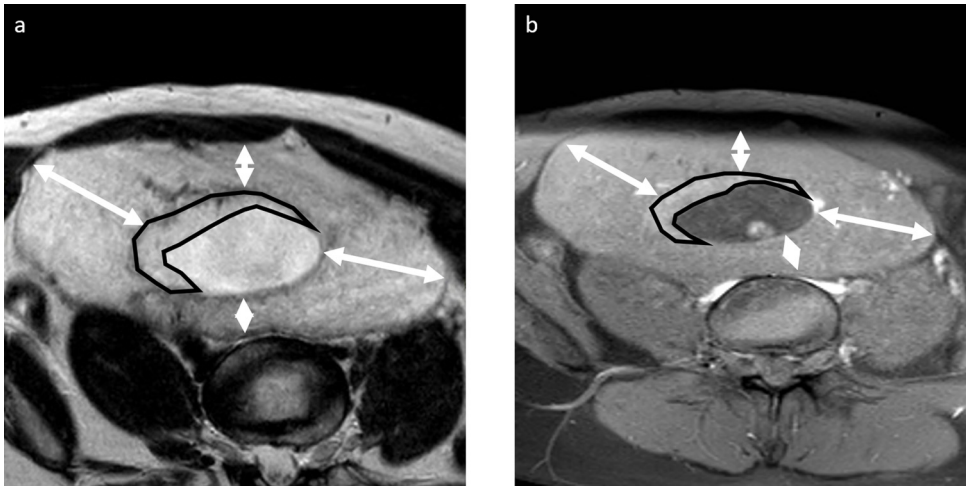

Fig. 2. Magnetic resonance imaging. T2-weighted image (a) and T1-weighted image (b) with inversion recovery in the axial plane of the uterus at 10 weeks of gestation. Diffuse T2 hyperintense and T1 slightly hyperintense (compared to muscle) myometrial thickening with T2 and T1 hypo-intense irregularities (White arrows in a and b). The placenta can be seen on the right side with anterior extension (black free form).

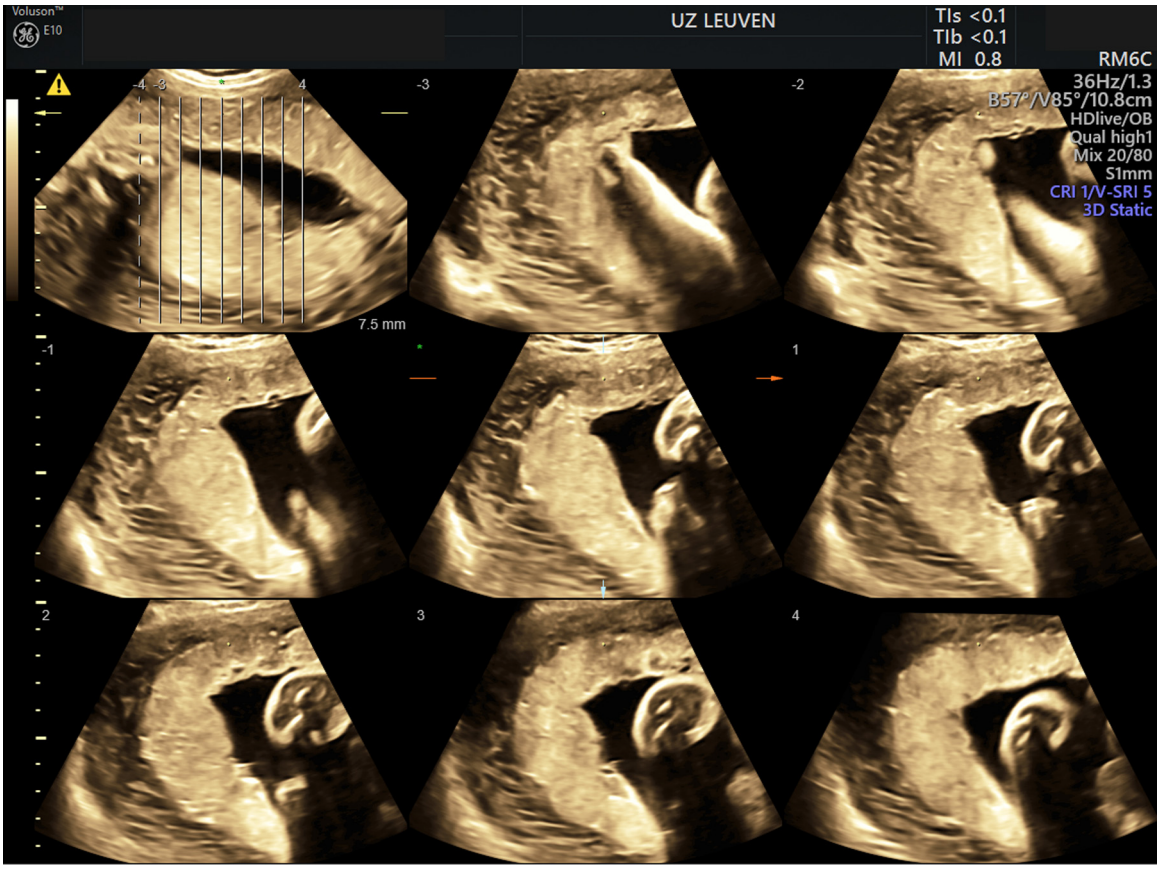

Fig. 3. Tomographic ultrasound imaging (TUI) – volume computer aided diagnosis (VCAD) ultrasound image at 32 weeks and 5 days.

hemangioma, one more patient underwent a hysterectomy at 17 weeks because of recurrent syncopes and the presumed risk of uterine rupture.

These numbers contrast with the undiagnosed group in which three out of the five patients (3/5, 60%) had a postpartum hemorrhage and a hysterectomy was necessary in all of them (3/3, 100%). There were no cases of maternal mortality in the group of antenatal diagnosed patients.

Discussion

Our literature search identified 15 cases of uterine hemangioma during pregnancy. High rates of complications were encountered, particularly a high rates of cesarian deliveries (67%), peripartum hemorrhage (53%) and ultimately hysterectomy for hemorrhage control (27%). Above and beyond the clear maternal risks, there is also significant fetal-neonatal morbidity as stillbirth was encountered in 13% of the cases.

In two thirds of patients (67%) the diagnosis was already made during pregnancy. In comparison to those with a postnatal diagnosis, these women had a lower incidence of postpartum hemorrhages (50% vs. 60% in the postpartum group) and peripartum hysterectomies (20% vs 100% in the postpartum group).

As far as we know, this is the first review reporting on uterine hemangioma and pregnancy outcomes. This review is limited to 15 case reports, with no uniform reporting or management. The lack of missing outcomes and heterogenous management greatly inhibits the interpretation of this review. Moreover, since it is clear from this review that uterine hemangioma can go unnoticed during pregnancy, it begs the questions whether there is an underreporting of uncomplicated cases leading to a publication bias.

Establishing the diagnosis of a uterine hemangioma before delivery seems beneficial for maternal outcome, as we found a lower number of postpartum hemorrhages and peripartum hysterectomies in this patient group. Therefore, we strongly encourage the routine systematic evaluation of the myometrium during standard second trimester anomaly ultrasound. An antenatal diagnosis allows for planning of the anticipated peripartum bleeding risk. On the one hand, antenatal diagnosis is relatively straightforward and can be made by standard 2D ultrasound. Once identified the patient can be referred to a tertiairy care center for more comprehensive care. On the other hand, this could lead to overtreatment, as in the case where a hysterectomy was performed at 17 weeks of gestation because of the assumed risk of uterine rupture. Furthermore, subsequent pregnancies may have a lower morbidity risk since only two of the multiparous women developed a severe postpartum hemorrhage and in only one a hysterectomy was performed. Yet, as previously mentioned, the obstetrical history was not routine reported upon.

Data are currently too limited to provide clear guidelines for the management of uterine hemangioma in pregnant women. It is also unclear whether additional imaging (i.e. MRI) beyond standard 2D ultrasound adds any diagnostic or management value. Therefore, we strongly recommend the establishment of an international registry for the reporting of all cases.

Conclusion

Although our current knowledge on uterine hemangioma during pregnancy is limited to 15 case reports, the condition seems to hold substantial risks for both mother and child. Therefore, these pregnancies should ideally be followed-up and cared for in centers of expertise. Routine screening for this clearly visible condition is feasible and routine systematic evaluation of the myometrium during standard

Table 1
Baseline patient characteristics and diagnostic data (VD = vaginal delivery; CS = cesarean section; GA = gestational age; Dx = diagnosis; PPH = postpartum hemorrhage; US = ultrasound; - = data not provided).

		Country	Age (y)	Gravidity	Previous VD	Previous CS	Pregnancy type	GA Dx (w)	Clinical presentation at Dx	Mode of Dx
1.	Aka et al. [2]	Ivory Coast	28	-(multiparous)	–	–	Singleton	Postpartum	Primary PPH with shock and DIC + secondary PPH	Histology (hysterectomy)
2.	Benjamin et al. [7]	Brunei	27	1	0	0	Singleton	Postpartum	Secondary PPH with shock	Histology (hysterectomy)
3.	Bhavsar et al. [1]	Philadelphia	25	1	0	0	Twins (NOS)	Postpartum	ARDS, pulmonary thromboembolism	Histology (autopsy)
4.	Comstock et al. [5]	United States	–	1	0	0	Singleton	27	Enlarged uterus	US + histology (myometrial biopsy)
5.	Dawood et al. [12]	Singapore	32	1	0	0	Singleton	Postpartum	Abdominal pain + dyspnea + anemia due to rupture of the hemangioma	Histology (excision hemangioma)
6.	Djunic et al. [8]	Serbia	33	1	0	0	Singleton	24	Referral for abnormal US + mild anemia	US + histology (myometrial biopsy)
7.	Gallegos et al. [13]	Mexico	–	–	–	–	–	16	Referral for abnormal US + anemia	US
8.	Lotgering et al. [14]	The Netherlands	32	1	0	0	Singleton	14	Enlarged uterus	US
9.	Milton et al. [15]	United Kingdom	25	2	0	0	Singleton	Preconceptionally	Severe menometrorrhagia	Pelvic arteriogram
10.	Reiffenstuhl et al. [16]	Germany	–	–	–	–	–	17	Enlarged uterus + recurrent syncopes	US + histology (hysterectomy)
11.	Sütterlin et al. [17]	Germany	26	2	1	0	Singleton	17	Referral for abnormal US + abdominal pain + enlarged uterus	US + histology (myometrial biopsy)
12.	Thanner et al. [9]	Germany	26	1	0	0	Singleton	18	Spotting + enlarged uterus	US + MRI + histology (myometrial biopsy)
13.	Uotila et al. [18]	Finland	25	1	0	0	Singleton	18	Enlarged uterus + abdominal pain + uterine contractions + anemia	US + MRI + histology (myometrial biopsy)
14.	Virk et al. [4]	United States	21	3	0	2	Singleton	Postpartum	Primary PPH	Histology (hysterectomy)
15.	Weissman et al. [19]	Israel	30	3	2	0	Singleton	33	Referral for abnormal US (asymptomatic)	US

Table 2
Pregnancy outcome, maternal and neonatal morbidity (GA = gestational age; VD = vaginal delivery; CS = cesarean section; PPH = postpartum hemorrhage, EBL = estimated blood loss; TOP = termination of pregnany; - = data not provided; NA = not applicable).

		Pregnancy complications	GA at delivery (w)	Labor onset	Delivery mode	PPH	EBL (mL)	Perinatal hysterectomy?	Maternal mortality	Birthweight (g)	Neonatal morbidity
1.	Aka et al. [2]	–	–	Spontaneous	VD	Yes	–	Yes (6 w)	No	2750	–
2.	Benjamin et al. [7]	None	–	–	Emergency CS	Yes	3000–4000	Yes (11 w)	No	–	Alive at discharge
3.	Bhavsar et al. [1]	–	–	–	Planned CS	–	–	No	Yes	–	–
4.	Comstock et al. [5]	None	40	–	Planned CS	Yes	1700	No	No	4025	–
5.	Dawood et al. [12]	Hemangioma rupture with stillbirth at 36 w	36	Spontaneous	Emergency CS	No	>1500	No	No	–	Stillbirth
6.	Djunic et al. [8]	Stillbirth at 28w	28	None	Emergency CS	No	–	No	No	–	Stillbirth
7.	Gallegos et al. [13]	–	38	–	Planned CS	Yes	–	Yes	No	–	–
8.	Lotgering et al. [14]	PPROM + preterm labor at 26w	35	Spontaneous	VD (vacuum)	Yes	1000	No	No	1880	–
9.	Milton et al. [15]	None	38	Spontaneous	VD	No	400	No	No	–	–
10.	Reiffenstuhl et al. [16]	None	17	TOP	Planned hysterectomy	No	–	No	No	–	–
11.	Sütterlin et al. [17]	None	41	None	Emergency CS	No	500	No	No	3320	Alive at discharge
12.	Thanner et al. [9]	Preterm labor at 32w	Term	Spontaneous	Emergency CS	Yes	–	No	No	3185	–
13.	Uotila et al. [18]	None	30	None	Emergency CS	Yes	>3000	No	No	1375	Respiratory problems
14.	Virk et al. [4]	None	–	None	Planned CS	Yes	2000	Yes	No	–	–
15.	Weissman et al. [19]	None	41	Spontaneous	VD	No	–	No	No	3535	Alive at discharge

second trimester anomaly ultrasound should be encouraged. An international registry for uterine hemangioma in pregnancy would be of great value to obtain better knowledge on this subject and could serve as a basis for the development of clinical management guidelines.

Authors' contribution

EB: Data curation, Formal analysis, Investigation, Methodology, Visualization, Writing – original draft, Writing – review & editing. MA: Visualization, Writing – original draft, Writing – review & editing. WF: Visualization, Writing – original draft, Writing – review & editing. JvdM: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Visualization, Writing – original draft, Writing – review & editing.

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Declaration of Competing Interest

No potential competing interest was reported by the authors.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jogoh.2022.102401.

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