Therapeutic strategies and challenges in the management of craniospinal tumours in pregnancy: a 10-year retrospective tertiary centre study, systematic review, and proposal of treatment algorithms

Prajwal Ghimire (✉ prajwal.ghimire@kcl.ac.uk)

King's College Hospital NHS Foundation Trust <https://orcid.org/0000-0003-2884-956X>

Graeme Pang

Jerry Philip

Sally Hazem

Kapil Rajwani

Jose Pedro Lavrador

Gordon Grahovac

Cristina Bleil

Nicholas Thomas

Richard Gullan

Francesco Vergani

Ranjeev Bhangoo

Keyoumars Ashkan

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Abstract

Objectives:

The study aims to evaluate therapeutic strategies in the management of craniospinal tumours in pregnant patients and the factors that influence the management along with their influence on maternal & foetal outcomes.

Materials and Methods:

A retrospective single-centre cohort study was performed at a tertiary neurosurgical referral centre. Pregnant patients referred to neuro-oncology multidisciplinary meeting (MDM) with craniospinal tumour were included. Ten-year patient data were collected from hospital records and neuro-oncology MDM outcomes. A systematic review was performed on the available literature in PubMed as per PRISMA guidelines.

Results:

Thirty-three patients were identified with a mean age of 31 years. 91%(n=30) had cranial lesions and 9% (n=3) had spinal lesions. Most of the patients had WHO Grade I/II tumours. 33.3% underwent surgery when pregnant whilst in 24.2% this was deferred until after the due date. 27.2% patients did not require surgical intervention and were followed up with serial imaging in the MDM. Left Lateral/park bench position was the preferred position for the spinal and posterior fossa lesions. Systematic review identified 26 eligible articles. Treatment algorithms are proposed addressing the therapeutic strategy for management of cranio-spinal tumours during pregnancy and the challenges for maternal and foetal outcomes were tabulated.

Conclusions:

Craniospinal tumours presenting in pregnancy are challenging. The surgical management needs to be tailored individually and as part of a multidisciplinary team approach. Maternal and foetal outcomes are to be considered during patient counselling.

Introduction

Craniospinal tumours presenting in pregnancy are rare despite primary intracranial tumours being the 5th leading cause of cancer-related death in women of age 20-39 years [1]. Primary malignant brain tumours in pregnant women occur in 26-150/million; meningioma comprises 13% of all CNS neoplasms identified during pregnancy with the incidence of around 7/million in the females in the 15-44 years age group; and vestibular schwannoma has an incidence of 17/10,000,000 in females aged 15-44 years [2,3,4]. Management of craniospinal tumours in pregnancy pose a considerable challenge to the neurosurgical community worldwide and requires a multidisciplinary team including neurosurgeons, neurologists, obstetrician, neuroradiologists and foetal medicine experts. Robust evidence-based guidelines are the current unmet need. This study aims to evaluate therapeutic strategies in the management of craniospinal tumours in pregnant patients and evaluate the factors that influence the management along with their consequence on maternal & foetal outcomes.

Materials And Methods

10-year Retrospective single centre Study

A retrospective single-centre cohort study was performed at a tertiary neurosurgical referral centre. Pregnant patients referred to our neuro-oncology multidisciplinary meeting (MDM) with craniospinal tumours were included. Ten-year patient data were collected from hospital records and neuro-oncology MDM outcomes between 2010-2020. All patients were discussed in neuro-oncology MDM. The inclusion criteria were pregnant patients with cranial and spinal tumours. Patients with craniospinal tumours operated prior to conception/pregnancy and craniospinal tumours diagnosed after delivery were excluded from the study.

Consent and Ethics Approval

All data collection were approved by the department of neurosurgery at the hospital. All data were collected retrospectively from patient records and thus did not require ethics committee approval. Patient consent for data collection were not required as it was retrospective, and all the images were anonymised.

Systematic Review

Systematic review with PRISMA guidelines was performed on data collected from PubMed (**Figure 1**). The systematic review has been registered in PROSPERO register with registration number **[BLINDED FOR REVIEW]**. Articles from 1950-2021 were searched on PubMed. The search strategy included *MeSH items*: ((Pregnancy OR Pregnant) AND (Glioma OR brain Tumour OR Meningioma OR Astrocytoma OR spinal tumour)). Two reviewers individually screened published papers based on inclusion and exclusion criteria and screened the title and abstract. Discrepancies was resolved by mutual consent obtained from

the third reviewer and data was extracted onto a standardized form designed in Microsoft Excel 2020. Data on management strategy, algorithms, risks factors, maternal and foetal outcomes were extracted.

Results

Results from 10-year retrospective Data:

The demographics of the patients treated at our centre are presented in **Table 1**. Thirty-three patients were identified with mean age of 31 years. 91% (n=30; supratentorial: 27, infratentorial: 3) had cranial lesions (pilocytic astrocytoma, prolactinoma, atypical pituitary adenoma, meningioma, glioblastoma, neurocytoma, hemangioblastoma, metastatic carcinoma, arachnoid cyst, tuberculoma, choroid plexus cyst) and 9% (n=3) had spinal lesions (schwannoma, ependymoma) (**Figure 2**). The majority (21/33; 63.6%) of the patients had WHO Grade I/II tumours. 33.3% (11/33) patients underwent surgery when pregnant whilst in 24.2% patients (8/33) this was deferred until after the due date. 27.2% patients did not require surgical intervention and were followed up with serial imaging in the MDM. 15.1% patients (5/33) proceeded to adjuvant therapy post-operatively. 43.4% (14/33) patients were referred to the obstetric team for elective/urgent caesarean-section (c-section) to facilitate tumour resection and there was 1 termination of pregnancy due to significant foetus-related events. Left Lateral/park bench position at surgery was preferred for the spinal and posterior fossa lesions.

Patients who did not require intervention and completed pregnancy

63.6% (21/33) patients did not require any intervention during pregnancy and completed the pregnancy. 8/21 required surgery post-partum (Meningioma, vestibular schwannoma, spinal myxopapillary ependymoma, central neurocytoma). 4/21 did not require further neurosurgical follow up (pineal cyst, non-specific changes, choroid plexus cyst) as deemed clinically insignificant. The 9/21 (27.2%) Lesions that were followed up with serial imaging post-delivery with further discussion in the neuro-oncology MDM were cortical dysplasia, arachnoid cyst, low grade glioma, cavernoma and DNET.

Patients who required treatment during pregnancy but with term delivery

15.1% (5/33) patients required surgical management during pregnancy and went on to have term delivery of the foetus (c-section/normal vaginal delivery). All the lesions were symptomatic low-grade lesions (Grade I/II) which included prolactinoma, hemangioblastoma, atypical pituitary adenoma, spinal ependymoma (Grade II, papillary) and spinal schwannoma. (Grade I). Patients were followed up post-delivery with imaging in the MDM. Non-contrast MRI imaging was the preferred post-operative imaging modality performed in cranial and spinal lesions within 24-48 hours after surgery. Obstetrician and foetal medicine experts were consulted pre-surgery, during the procedure and post procedure to monitor foetal wellbeing with ultrasonography and cardiotocography (CTG).

Patients who required treatment during pregnancy but with pre-term delivery

6/33 patients underwent surgical management during pregnancy. There was post-neurosurgical pre-term delivery of the foetus in 5/33 patients through c-section managed by the obstetric/ neonatal team. No infant deaths were reported within the first 30 days of delivery. In this group, 3/6 patients had high grade lesions (Glioblastoma WHO Grade IV.). 1/6 patient underwent endoscopic third ventriculostomy for obstructive hydrocephalus secondary to posterior fossa pilocytic astrocytoma Grade I and the tumour was later resected post-delivery. 1/6 patient had sellar apoplexy secondary to prolactinoma requiring trans-nasal transsphenoidal approach for decompression of the optic apparatus. 1/6 patient (metastatic carcinoma from the lung) required termination of pregnancy prior to craniotomy and proceeded to adjuvant treatment. Decision was made with MDT discussion with a patient centred approach.

Systematic Review

Systematic review identified 26 eligible articles which were filtered through the inclusion and exclusion criteria as per PRISMA guidelines. Among these, 4 studies contained algorithms for trimester-based management of pregnant patients with brain tumour (general), glioma, meningioma, and skull base tumours but no article was identified that demonstrated an algorithm for management of spinal tumours. Glioma algorithm proposed by Peteers S et al was the only algorithm in the literature to address management of glioma diagnosed during pregnancy, antiepileptics management, post-delivery management and management of glioma diagnosed prior to pregnancy. They stratified their strategy based on the definition of stable/low grade glioma and unstable/progressive/high-grade glioma. The relevant articles proposing algorithms were summarised on to a tabulated form (**Table 2**). Articles discussing management of craniospinal tumours with their conclusion and recommendations were tabulated in **Table 3**.

Algorithms

We propose two algorithms addressing the therapeutic strategy for management of cranial (**Figure 3**) and spinal tumours (**Figure 4**) in the first, second and third trimesters of pregnancy. These proposed algorithms address important factors in the management of these complex scenarios, which have not been described in the literature in a single flow diagram before, including multidisciplinary discussion, surgical management, adjuvant treatment/radiotherapy, antiepileptic and steroids management, counselling regarding termination of pregnancy, progression of pregnancy with monitoring, decision making for planned caesarean section or supervised vaginal delivery.

Challenges

The challenges and factors that influenced the maternal and foetal outcomes during management of these craniospinal tumours in pregnancy were identified from our data and the systematic literature review. These have been tabulated in **Table 4**.

Discussion

This single-centre retrospective study provided an overview of the strategies available for the management of different subtypes of craniospinal tumours presenting during pregnancy, depending on their presentation, clinical and imaging findings. The range of presentations varied from incidental findings on imaging such as arachnoid cyst/pineal cyst/meningioma to extreme emergencies such as a patient in coma with the imaging suggestive of a contrast enhancing high grade tumour such as a glioblastoma. All patients underwent referral to the neuro-oncology MDT and consensus was obtained for management which was then recommended to the referring physician/oncologist. Patients considered as candidates for surgical management, other than those requiring emergency admission, were advised on AEDs, steroids and were seen in the pre-assessment clinic where imaging findings and surgical management options were discussed with the patients and family. This was then followed by the patient being offered a date for surgery and anaesthetic assessment with routine pre-operative investigations including haematological profile, lower limb dopplers and further MRI imaging as deemed necessary. Non-contrast imaging was obtained in all patients requiring surgery whilst being pregnant.

In the absence of prospective large data sets, our experience combined with the information gathered from the literature, constitute useful guidelines in the management of these patients.

Cranial Tumours in Pregnancy

Studies have demonstrated that tailored individualised case-based protocol for the treatment of brain tumours during pregnancy can allow term delivery with even the possibility of safe vaginal delivery of the

foetus[2,5,6,7,8].

Glioma and Pregnancy

Pregnancy does not seem to influence the clinical course of glioma patients nor impact the delivered children's health [9]. However, a population-based case control study demonstrated a decreased glioma risk associated with ever-pregnancy compared with never-pregnancy and that breast feeding among parous women increased glioma risk, concluding that reproductive hormones may influence the occurrence of glioma [5]. Findings from observational studies show that there is no known effect of pregnancy on survival in low-grade glioma patients although pregnancy can provoke clinical deterioration and tumour growth on MRI. In symptomatically stable women at term, there is no benefit of caesarean section over vaginal delivery with respect to adverse events in mother or child. Unanswered questions in literature include when pregnancy should be discouraged, what the best monitoring schedule is for both mother and the foetus, and if/ how chemo- and radiation therapy can be safely administered during pregnancy[4]. Ronning et al demonstrated that pregnancy did not seem to influence the overall survival in patients with low grade glioma who became pregnant[7]. However, the recommendation was that the prospective mothers must also be thoroughly informed about the reduced expected overall survival associated with low grade glioma, regardless of the decision to become pregnant[7].

High grade Glioma

Glioblastoma although rare can present as a neurological emergency requiring surgery during pregnancy. A case report by Mackenzie et al described a patient undergoing caesarean section for delivery at 36+2 weeks followed by craniotomy for resection of GBM and then radiotherapy and chemotherapy post-partum[10]. A literature review in 2012 discussed the effects of radiation during CT imaging, chemotherapy during second and third trimester, timing of surgery and delivery of pregnancy, post-operative management of pregnancy in neurosurgical patients, anaesthetic considerations, use of anticonvulsants and steroids [11]. The paper suggested that adjuvant therapy (chemo-, radiotherapy) in pregnancy was likely to cause deleterious effects ranging from intrauterine growth retardation, low birth weight, premature delivery and still birth [11]. Detailed discussion with the patient regarding potential adverse outcome and uncertainty was recommended to be carried out in conjunction with the oncologist. There was an increased risk of miscarriage associated with surgery in the first trimester and some evidence for increased risk of birth defects [11]. The proposal therefore was that surgery should be delayed until second trimester whenever possible [11]. The study also highlighted the co-ordination within the multidisciplinary team and suggested individualised approach for each patient during the tumour and pregnancy management [11]. An early population-based assessment demonstrated that the observed to expected ratios were substantially reduced for brain malignancy and meningioma and thus, rejected the

view that intracranial neoplasms presented more often during pregnancy[2]. This led to the current recommendations on individualised MDT based approach to different types of cranial tumours in pregnancy[2].

Meningioma and Pregnancy

Risk of meningiomas in women <50 years was increased with an increase in number of pregnancies as compared to nulliparous women [5], concluding the influence on the occurrence of meningiomas by reproductive hormones. Reports of shrinkage or disappearances of meningiomas after pregnancy suggest that repeat imaging should be performed during pre-operative assessment. Acceleration of growth rates during increased levels of serum oestrogen (O) and progesterone (P) in pregnancy have been demonstrated with overexpression of O/P receptors [12]. Large symptomatic meningiomas require surgical resection regardless of the status of pregnancy; preferred timing of intervention is, however, a matter of debate. Surgical resection during pregnancy may be associated with maternal and foetal morbidities/mortalities but overall outcomes are similar to post-partum resections for the mother. Patients with pregnancy >27 weeks are likely to undergo foetal delivery first followed by planned tumour resection. Maternal health and well-being are paramount in the decision-making process but aiming for term delivery has been shown to avoid prematurity associated complications in the neonate [13]. A systematic review demonstrated similar incidence of meningiomas in pregnant and non-pregnant women; symptoms flare up is likely during pregnancy due to fluid retention, engorgement of vessels, and presence of sex hormone receptors in the tumour cells. Foetal monitoring by biophysical profile (ultrasound, amniotic fluid volume, foetal breathing movements) and cardiotocography (CTG) is recommended [8]. Surgery is the preferred choice of treatment for meningiomas, but individualised approach is recommended. Foetal biophysical profile scoring system, Umbilical arterial Doppler assessment, neuro-anaesthesia, and microsurgical techniques permit safe neurosurgical management of meningiomas and other brain tumours during pregnancy. Emergency surgical intervention should be reserved for patients with fast tumour growth rates, active hydrocephalus requiring shunting, signs of impending brain herniation, or progressive neurological deficits [8].

Other Cranial tumours and Pregnancy

A case series published in 2019 reported sellar region lesions that underwent surgical resection in four patients, diagnosed during pregnancy, presenting with deterioration in vision. All patients continued their pregnancy to term post operatively. They concluded that MDM guided decision-making process, leading to surgical resection of sellar region lesions in pregnant women with severe impairment, was the key to the positive outcome of pregnancy [14]. Priddy et al have suggested an algorithm for management of symptomatic benign skull base tumours and have highlighted red flag symptoms of paresis, complete

visual loss, brain herniation, complete III nerve palsy and coma as needing emergency surgery. Trimester based management was highlighted in this series and discussion regarding continuation vs termination of pregnancy was considered for patients diagnosed in the first trimester of pregnancy. Postponement of surgery as far as safely possible was suggested for patients in second and 3rd trimester [15].

Spinal tumours and Pregnancy

The number of meningiomas tends to increase during pregnancy with gliomas and spinal vascular tumours more commonly diagnosed in the first and third trimesters. Postpartum amelioration of symptoms has been described in meningiomas and spinal vascular tumours such as haemangiomas [16]. Another case series of 21 pregnant patients with spinal tumours suggested that surgery for benign spinal tumours could be postponed till after the delivery. The indication for surgery during pregnancy include highly malignant tumours or rapid deterioration in neurological function. Avoiding radiotherapy and chemotherapy as far as possible is safer during pregnancy for these tumours [17]. Bitterman et al reported a case of ependymoma resected at 20 weeks of pregnancy and focused on post-operative rehabilitation whilst being pregnant [18]. It highlighted the impact on foetus, delivery, and neonatal complications. It suggested that vaginal delivery was possible even when spinal cord intrinsic tumour had been resected with residual neurology. There was increased risk of pressure injuries, bladder dysfunction (neurogenic bladder) and autonomic dysreflexia and lesions at T6 and above were prone to autonomic dysreflexia leading fetal complications such as fetal hypoxemia and fetal bradycardia [18]. Difficulties in sensation of fetal movement and uterine contractions can occur in patients with lesions above T11 [18].

Our retrospective study and the systematic review of the current literature demonstrated that there is an unmet need for uniform management guidelines for craniospinal tumours in pregnancy. There is no level 1 evidence with regards to management options or timing of surgery. Majority of the eligible articles identified in the systematic review were retrospective studies. In this paper, we have now addressed this unmet need with algorithms for both cranial and spinal tumours in pregnancy along with identification of factors that would play a key role in maternal and foetal outcomes during management of these tumours. These factors will play a crucial role in the decision-making process regarding whether to operate or not to operate and, when to offer surgery, for these high risk, complex patients.

Limitations

Our data was based on a retrospective series with modest numbers. Further large-sample size prospective studies would provide robust evidence regarding management of pregnant patients with craniospinal

tumours.

Conclusion

Craniospinal tumours in pregnancy are under-reported and difficult to manage. The surgical management should be tailored to different types of tumours with a unique multidisciplinary approach. Maternal and foetal outcomes are to be considered during patient counselling. Benign tumours/lesions could be observed; malignant tumours/tumour producing mass effect should be considered for debulking. Spinal tumours producing progressive neurological deficits should be considered for debulking/resection.

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Tables

Table 1: Demographics of 10-year retrospective patient cohort

Demographics		Data
Number of Patients		33
Mean age (years)(range)		31 (24-43)
Histology		
Cranial	WHO Grade	91% (n=30)
Pilocytic astrocytoma	I	1
Meningioma	I	7
Glioblastoma	IV	3
Atypical Pituitary adenoma		2
Prolactinoma (apoplexy)		1
Vestibular Schwannoma	I	1
Metastatic Carcinoma		1
Low Grade Glioma	I/II	3
DNET	I	1
Central neurocytoma	I	1
Hemangioblastoma	I	1
Tuberculoma		1
Choroid plexus cyst		1
Cavernoma		1
Pineal cyst		1
Cortical Dysplasia		1
Non-specific cortical changes		1
Arachnoid cyst		2
Spinal		9% (n=3)
Papillary Ependymoma		1
Myxopapillary Ependymoma		1
Schwannoma		1
Trimester at diagnosis		

First	12% (n=4)
Second	45.5%(n=15)
Third	42.5%(n=14)
Surgical treatment during pregnancy Resection/debulking	
<i>Endoscopic third ventriculostomy (ETV)</i>	30.3%(n=10)
No intervention	3.1%(n=1)
	66.6%(n=22)
Timing of Surgery (Trimester)	
First	2
Second	4
Third	5

Table 2: Studies proposing algorithms for management of craniospinal tumours in pregnancy ^{13,15,19,20}

Articles	Management of Pathologies addressed	No of cases	Evidence	Type of Study	Approach
1. Ng et al. 2008	Brain tumours Subarachnoid haemorrhage, AVM, cerebral aneurysm Back pain Disc herniation	N/A	IV	Literature review	Trimester based
2. Priddy et al, 2018	Skull base tumours -Grade I/II meningioma/schwannoma -Adenoid cystic carcinoma -mucocele -pituitary adenoma	9	IV	Case series	Trimester based
3. Peeters et al, 2018	Glioma (WHO Grade II-IV)	50	IV	Multi-institutional retrospective study/Case Series	Trimester based
4. Laviv et al, 2018	Meningioma	104	III	Systematic review	Trimester based

Table 3: Characteristics of studies included in systematic review

Articles	No. of patients	Type of study	Pathologies addressed	WHO Grade	Recommendations
1. Girault et al, 2014 ²¹	20	Retrospective cohort study	Oligodendroglioma Meningioma CP angle chondroma Arachnoid cyst Glioblastoma Astrocytoma Neurocytoma DNET Pineoblastoma Glioma Craniopharyngioma	I-IV	Poor perinatal outcome and maternal death were associated with brain tumours diagnosed during pregnancy. Vaginal delivery with epidural analgesia can be performed in these groups.
2. Lynch et al, 2011 ²²	10	Case series and literature review	Melanoma metastasis Meningioma Epidermoid Chemodectoma Oligodendroglioma Astrocytoma Pituitary Adenoma	I-IV	The timing of craniotomy and the resection of the tumour will depend of the mother's neurological condition, the tumour histological type as well as the gestational age. A multi-disciplinary approach was used to determine the optimal management for each patient.
3. Cohen-Gadol et al, 2009 ³	34	Case series and review of literature	Vascular lesions (aneurysm, dAVF, cavernous malformation) GBM Astrocytoma Meningioma	I-IV	Surgery for intracranial lesions in pregnant patients is generally well tolerated by both mother and fetus. Preoperative delivery by

			<p>Infiltrative pineal tumour</p> <p>Thalamic tumour</p> <p>Oligodendroglioma</p> <p>Cerebellar hemangioblastoma</p>		<p>cesarean section of term or near-term babies is reasonable.</p> <p>Some patients treated conservatively may deteriorate and require an urgent surgery.</p>
4. Mackenzie et al, 2005 ¹⁰	1	Case report and literature review	GBM	IV	GBM, rare diagnosis during pregnancy, may present as a neurosurgical emergency.
5. Jayasekera et al, 2012 ¹¹	N/A	Review of literature	GBM	IV	<p>In planning treatment, potential benefits to the mother must be balanced against the risks to the foetus.</p> <p>Evidence relating to timing of surgery and the use of radiotherapy and chemotherapy in pregnancy is limited.</p> <p>Management of peritumoral oedema and seizures in pregnancy is complicated by the potential for drug-related teratogenic effects and adverse neonatal outcomes on the foetus.</p> <p>The general anaesthetic used for surgery must</p>

					factor obstetric and neurosurgical considerations.
6. Haas et al, 1986 ²	29	Case series and literature review	GBM Astrocytoma Ependymoma Meningioma Acoustic Neurinoma Pituitary adenoma AVM Sarcoma	I-IV	This review did not provide support for the view that intracranial neoplasms present more often during pregnancy.
7. Forster et al, 2019 ⁹	18	Case series and literature review	Astrocytoma Oligodendroglioma Ependymoma	I-III	Pregnancy does not seem to influence the clinical course of glioma patients. Glioma seems not to have an impact on delivered children's health.
8. Van Westrhenen et al, 2018 ⁴	316	Systematic review	Astrocytoma Oligodendroglioma Glioblastoma Gliosarcoma Oligoastrocytoma	I-IV	There is no known effect of pregnancy on survival in low-grade glioma patients. Pregnancy can provoke clinical deterioration and tumour growth on MRI. In stable women at term, there is no benefit of caesarean section over vaginal delivery, with

					respect to adverse events in mother or child.
9. Bonfield et al, 2012 ²³	NA	Literature review	<p>Intracranial neoplasms</p> <p>Low- and high-grade glioma</p> <p>Meningioma</p> <p>Pituitary tumours</p> <p>Acoustic Neuroma</p>	I-IV	<p>Brain tumours are uncommon in pregnant patients.</p> <p>Women of childbearing age with brain tumours require specific counselling about the medical risks of pregnancy as determined by the histology, location, and biologic characteristics of their tumour.</p> <p>MRI is safe in pregnancy, generally performed without intravenous contrast.</p> <p>Pregnancy is generally not a contraindication to surgical resection or brain tumour biopsy, although it is often a contraindication to radiation therapy and always a contraindication to systemic chemotherapy.</p> <p>Because of potential increase of ICP during Valsalva manoeuvre in a patient with a brain tumour, caesarean section</p>

					is usually preferable to vaginal delivery once the foetus is term or near term.
10. Yust-Katz et al, 2014 ²⁴	15	Retrospective cohort/case series	Glioma	II-IV	In contrast to grade I gliomas, the tumour biology of grades II and III gliomas may be altered during pregnancy, leading to an increased risk of tumour progression; supporting the need for increased tumour surveillance and patient counselling.
11. Ronning et al, 2016 ⁷	65 (that gave birth after diagnosis) 281 (that did not give birth after diagnosis)	Retrospective cohort study on registry data	LGG	I-II	Pregnancy does not seem to have an impact on the survival of female patients with LGG.
12. Wigertz et al, 2008 ⁵	1532	Population based case control study	Glioma Meningioma	I-IV	Reproductive hormones may influence the occurrence of meningioma and glioma.
13. Chakravarthy et al, 2018 ¹²	1	Case report and literature review	Meningioma/Houndini Tumour	NA	Because meningioma shrinkage or disappearance may occur after pregnancy, repeat imaging is advised as part of a preoperative evaluation. It is possible that an undetermined amount of meningioma removal surgeries may be avoided

					with further research into monitoring hormone levels connected to meningioma growth.
14. Verheecke et al, 2014 ⁶	27	Case series and literature review	Primary brain tumours Meningioma Brain metastasis	I-IV	<p>Treatment of brain tumours during pregnancy is feasible.</p> <p>The children of the ongoing pregnancies were live births and main risks were mostly related to preterm birth.</p> <p>The timing of the different treatment options should be coordinated for each patient in an MDM based on the available evidence and experience.</p> <p>Treatment according to standard protocols including surgery, radiotherapy, and chemotherapy, during pregnancy, appears to allow a term delivery and a higher probability of a vaginal delivery.</p>
15. Dumitru et al, 2021 ⁸	NA	Systematic review	Meningioma	N/A	There is similar incidence of meningioma in pregnant and non-pregnant women

					<p>Symptoms might flare during pregnancy due to water retention, engorgement of vessels, and the presence of sex hormone receptors on tumour cells.</p> <p>Meningioma may impact the route of pregnancy with adverse effects on the foetus.</p> <p>Foetal monitoring by biophysical profile and CTG is needed.</p> <p>The preferred treatment option is surgery, but gestational age and the woman's status must be taken into consideration.</p>
16. Zwinkels et al, 2013 ²⁵	7	Case Series and literature review	<p>Glioma</p> <p>(Astrocytoma</p> <p>Oligoastrocytoma</p> <p>PXA</p> <p>Ependymoma)</p>	II-III	<p>If a patient with a glioma expresses the wish to become pregnant, we advise for counselling her and her partner on the risks of tumour progression and malignant transformation during the pregnancy by a multidisciplinary team (neurologist, neurosurgeon, obstetrician, paediatrician, anaesthesiologist).</p> <p>In case of assisted reproduction</p>

techniques like IVF in women already carrying a glioma, we advise against hormonal stimulation considering the potential effects of progesterone and gonadotropin hormones on tumour growth and dedifferentiation.

MRI with contrast agents can be safely performed during pregnancy, preferentially after 12–16 weeks of gestation.

In case of tumour progression necessitating treatment during the first or early second trimester of pregnancy, a therapeutic abortion at that time is still feasible.

A follow-up MRI as a routine procedure is advised at 32–36 weeks of gestation. The advantage of such timing of neuroimaging is close monitoring of tumour progression without undue risks for the unborn child, and that both induction of labour and tumour therapy can be initiated if necessary.

					Depending on the hazards of increased ICP during delivery, an elective caesarean delivery rather than a vaginal delivery should be considered, provided that foetal pulmonary maturity can safely be assumed.
17. Casabella et al, 2017 ²⁶	1	Case report and literature review	Foramen Magnum Meningioma	I	<p>We believe a three fourths prone position of a pregnant patient is safe and adequate for the far-lateral exposure of craniocervical lesions.</p> <p>Rapid growing of tumour can be precipitated by steroids management during pregnancy.</p>
18. Roelvink et al, 1987 ¹⁶	3	Case series and Literature review	Medulloblastoma Cerebellar Astrocytoma Spinal Intramedullary astrocytoma	I-IV	<p>The incidence of brain tumours that become symptomatic during pregnancy appears to be decreased compared with that in age-matched women.</p> <p>The relative frequency of the different primary brain tumour types is not changed by pregnancy.</p>

					<p>The number of meningiomas gradually tends to increase during pregnancy, with gliomas and spinal vascular tumours accumulating in the first and third trimesters, respectively.</p> <p>Postpartum amelioration of symptoms has especially been described for meningiomas and spinal vascular tumours.</p>
19. Meng et al, 2015 ¹⁷	21	Case Series and literature review	<p>Spinal Tumours</p> <ul style="list-style-type: none"> -Schwannoma -Haemangioma -Multiple myeloma -Metastatic tumour -Eosinophilic Granuloma -Giant Cell Tumour 	I-IV	<p>With close observation, it was found that most of pregnant patients with benign spine tumours could postpone surgery after delivery.</p> <p>Surgical treatment should be adopted during pregnancy when patients are with highly malignant tumour or experience a sharp deterioration.</p>
20. Bitterman et al, 2019 ¹⁸	1	Case report and literature review	Spinal cord Ependymoma	N/A	<p>Providers should not assume all pregnant women with low back pain have gestational back pain, as it can be due to more insidious causes.</p> <p>The rehabilitation course for women who develop an SCD during gestation should</p>

					be carefully tailored toward their pre- and post-natal care and with the education of how the disorder can affect pregnancy and parenting.
21. Zhong et al, 2019 ¹⁴	4	Case series and literature review	Sellar Tumours -Tuberculum sellae Meningioma -Pituitary adenoma -Pituitary Abscess	I-II	With the MDT guiding the decision-making process, surgical resection of sellar region SOLs in pregnant women with severe visual impairment is practical to improve the prognosis without affecting the outcomes of pregnancy for either the mother or the infant.
22. Terry et al, 2012 ²⁷	860	Retrospective cohort population study	CNS Neoplasms -Malignant brain tumour -Benign brain tumours -Spinal Tumours	I-IV	Malignant brain tumours were associated with adverse pregnancy outcomes CNS neoplasms were associated with higher rates of caesarean delivery.

GBM: Glioblastoma; ICP: intracranial pressure; CNS: central nervous system; SOLs: space occupying lesions; SCD: spinal cord disease

Table 4: Challenges/factors influencing maternal and foetal outcomes during management of craniospinal tumours in pregnancy (Bitterman 2019, Terry 2012, Dumitru 2021, Zwinkels et al, 2013)

Factors/Challenges
1. Tumour related factors <ul style="list-style-type: none"> -Grade of Tumour (Grade 1/II vs Grade III/IV) -Cell origin (e.g.: Meningioma/spinal ependymoma/ hemangioblastoma/pituitary macroadenoma) -Location of Spinal Tumour (IDEM vs IDIM) -MGMT Methylation/IDH mutation/3p19q co-deletion -Management of hydrocephalus (VP shunt vs ETV vs External ventricular drainage)
2. Pregnancy related factors <ul style="list-style-type: none"> -Stage of Pregnancy (first vs second vs third trimester) -Eclampsia/Seizures -Twin Pregnancy (Pre-term delivery) -Positioning during spinal surgery
3. Treatment related factors <ul style="list-style-type: none"> -Antiepileptics (Avoid Phenytoin, Na Valproate) -Mannitol/hypertonic saline (avoid Mannitol except in emergency) -Chemotherapy -Radiotherapy -Anaesthesia (Volatiles vs TIVA vs Spinal; Avoid spinal anaesthesia in intrinsic cord tumour with syringomyelia) -Pain management (Paracetamol vs Gabapentin/Pregabalin vs amitriptyline)
4. Imaging related factors <ul style="list-style-type: none"> -CT Scan (radiation) -MRI (? first trimester MRI effects) -PET (radiation) -Intra-operative ultrasound (localisation of level in spinal lesions; assess vascularity pre-resection)
5. Co-morbidities <ul style="list-style-type: none"> -Metastatic disease (Adjuvant treatment: CT/RT)
6. Performance Status at tumour diagnosis

TIVA: Total intravenous anaesthesia; CT: chemotherapy; RT: radiotherapy; IDEM: intradural extramedullary; IDIM: intradural intramedullary; VP: ventriculoperitoneal; ETV: endoscopic third ventriculostomy; MRI: magnetic resonance imaging; CT scan: Computerised tomography; PET: positron emission tomography; IDH: isocitrate dehydrogenase; MGMT: O6-methylguanine DNA-methyltransferase

Figures

Figure 1: PRISMA flowchart for systematic Review

Figure 1

: PRISMA flowchart for systematic Review

Figure 2

Examples of different craniospinal tumours from the retrospective study

a: Sagittal MRI T2 image showing T12-L1 intradural extramedullary lesion causing complete obliteration of the canal diameter with conus compression **b.** T2 Axial and T1 post Gadolinium MR image showing large right frontal contrast enhancing lesion with mass effect, midline shift and ventricular compression (Histology: WHO Grade IV Glioblastoma) **c.** Coronal, sagittal and axial T1 post gadolinium MRI images showing large cerebellar cystic-solid lesion with contrast enhancing solid component with compression of the fourth ventricle producing obstructive hydrocephalus; flow voids seen in the solid component. **d:** intra-operative image of patient on image a showing extramedullary intradural tumour being resected with its relations to the conus and the nerve roots (Histology: WHO grade I schwannoma) **e:** intraoperative ultrasound image demonstrating increased vascularity of the lesion demonstrated in image c indicating highly vascular lesion (Histology: Hemangioblastoma)

Figure 2: Proposed Algorithm for therapeutic strategy for Cranial tumours in pregnancy

Figure 3

Algorithm for therapeutic strategy for Cranial tumours in pregnancy

Figure 3: Proposed Algorithm for therapeutic strategy for spinal tumours in pregnancy

Figure 4

Algorithm for therapeutic strategy for spinal tumours in pregnancy