

Headache in Pregnancy: An Overview of Differential Diagnoses

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Abstract

Headache is a common symptom in pregnancy, reported in up to 35% of women during their antenatal period. During pregnancy, women may experience their first episodes of headache, which could become a recurrent problem. The purpose of this review is to recognise the classical presentation and contributory factors of primary and secondary headaches. Primary headaches include tension type headache and migraine. Secondary headaches include hypertension, pre-eclampsia, idiopathic intracranial hypertension, subarachnoid haemorrhage, cerebral venous thrombosis, and reversible cerebral vasoconstriction syndrome. As we encounter headaches so frequently in patients who are pregnant, we need to equip ourselves to recognise the 'red flag' signs that would alert practitioners to the need for urgent management and differentiate it from those that are benign.

This article will cover the following topics:

- Primary Headaches
 - Tension Type Headache
 - Migraine
- Secondary Headaches
 - Hypertension/Pre-Eclampsia
 - Idiopathic Intracranial Hypertension o Subarachnoid haemorrhage
 - Cerebral Venous Thrombosis
 - Reversible Cerebral Vasoconstriction Syndrome
- Assessment of patients with headache
- Red Flag Signs

Keywords: Headache; Pregnancy; Tension; Migraine

Introduction

Headache is a common presenting complaint in pregnancy. For some women it may be their first encounter of significant headaches. The majority of headaches are benign and settle with conservative treatments, such as simple analgesia. However it is crucial to be able to differentiate headaches that are benign from those that are secondary to conditions that predispose patients to a higher risk of morbidity and mortality. Headaches may be an initial symptom of a life threatening condition, such as Central Venous Thrombosis (CVT). Consequently, headache in pregnancy can cause much anxiety, not only for the patient but also for the attending clinicians. It is important that pregnant women presenting with headache are thoroughly assessed and investigated in order to rule out any serious underlying pathology.

The International Headache Society (IHD) classifies headaches as either primary or secondary. Primary headaches are benign and have no underlying medical problem associated with them. Examples include Tension Type Headache (TTH) and Migraines. Secondary Headaches occur as a result of medical conditions such as hypertension, pre-eclampsia, idiopathic intracranial hypertension, subarachnoid haemorrhage, cerebral venous thrombosis and reversible cerebral vasoconstriction syndrome.

We will briefly describe the typical presentation and clinical features of the different types of headache.

Primary headaches

Primary headaches can be considered benign and are not the

consequence of a predisposing medical condition. These headaches generally improve during pregnancy and pose no significant risk to the pregnancy [1,2]. The IHD includes the following conditions as primary headaches:

- Tension Type Headaches (TTH)
- Migraine
- Cluster Headache
- Other Primary Headaches [3]

This article will only discuss TTH and Migraines as these are the most commonly encountered primary headaches in pregnancy.

Tension type headache (TTH)

Tension headaches are extremely common and have a lifetime prevalence of up to 88% in women [4]. TTH is thought to be secondary

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to muscle contraction, however the exact mechanism is not fully understood. TTH can be related to periods of stress [1]. It can be further differentiated into frequent, infrequent, chronic and probable TTH depending on the timing and chronicity of the episodes [3]. TTH is the most common headache encountered in pregnancy and women may classically present with the following features:

- Bilateral Headache
- Tight, band-like pain
- No associated aura

Patients with TTH will not have the pain worsened by physical activity and will have no abnormal findings on neurological examination [1,3,4]. TTH poses no risk to the developing pregnancy, and limited studies propose that episodes of TTH decrease during pregnancy [2]. TTH can be managed with simple over the counter analgesics, such as paracetamol and codeine. Non-Steroidal Anti-Inflammatory Agents (NSAIDs) are contraindicated during pregnancy.

Migraine

Migraine is a common disorder characterised by a unilateral headache that is throbbing and pulsating in nature and can be associated with aura [3]. Migraines are three times more common in women than in men [1] and occur with the greatest frequency in the childbearing years [5]. Migraines will therefore affect the care of many pregnant women. The pathogenesis of migraine, though largely uncertain, is correlated with cerebral vasculature vasodilatation, serotonin release and stimulation of nociceptors [1]. Migraine can be precipitated by a single or combination of trigger factors. These can include dietary triggers, such as chocolate and cheese, stress, and hormonal influences [1,3,4]. Women who suffer with migraines around the time of menarche tend to have a reduction in migraine episodes during pregnancy. Migraine can present for the first time in pregnancy.

The IHCS classifies migraine into two categories, either being associated with aura or without aura [3]. The presenting features of a migraine headache are as follows:

- Unilateral headache
- Throbbing/Pulsating nature
- Moderate intensity
- Worsened by any physical activity
- Associated with either photophobia or phonophobia
- Nausea or vomiting present [1,3,4,5]

Migraines are commonly described over 4 phases, having an initial prodromal phase, followed by aura, headache and the post-dromal phase [4]. The prodromal phase can have an onset of hours before the headache, and can include numerous sensory symptoms, such as hemianopia, dysphasia, photophobia and phonophobia [1,4]. This is followed by the classical aura, which usually occurs just before or at the same time as the headache. It includes the visual symptoms scotoma, fortification spectra, specks and flashes, as well as generalised sensory symptoms such as paraesthesia. This is followed by the classic headache described above and the post-dromal phase.

Migraine most commonly improves in pregnancy, especially during the second and third trimesters [1,6]. Some studies have shown that women who suffer with migraines are at increased risk of pre-eclampsia, and therefore it is of great importance to monitor their

blood pressure and obtain a urine dipstick [1,5]. Studies also report that women who suffer with migraine without aura have better symptom control during pregnancy [7,8].

Neurological examination of a pregnant woman with a migraine is usually equivocal. The prodromal and aura symptoms may lead to focal neurological signs, such as reduced sensation and, in cases of hemiplegic migraine, focal weakness. In these cases it is extremely important that full investigations are carried out in order to rule out other underlying causes of headache. It is very difficult in these clinical situations to differentiate between hemiplegic migraine and other differential diagnoses, such as CVT or transient ischaemic attacks [1].

Acute migraine can be managed with conservative measures, such as analgesia, hydration and anti-emetics. Paracetamol and codeine are most commonly used as they are deemed the least harmful during pregnancy. NSAIDs, such as ibuprofen, are contraindicated, especially in the third trimester, as they can cause premature closure of the patent ductus arteriosus [8]. Serotonin receptor antagonists (Triptans), such as Sumatriptan, are used commonly in the non-pregnant population to treat migraines. There is limited evidence regarding the safety of triptans during pregnancy. There is the most amount of evidence for the use of Sumatriptan, which can be considered in severe migraines non responsive to simple analgesics [5,8].

Patients suffering with recurrent migraines during pregnancy should be considered for prophylactic treatment. Simple methods include avoiding triggers, ensuring a good sleep and nutrition pattern with moderate exercise and relaxation [9]. Non-pharmacological methods include biofeedback relaxation techniques and acupuncture. Both of these methods have evidence to reduce migraine frequency in the non-pregnant population and therefore could be applied to the pregnant population [9]. Pharmacological agents employed for prophylaxis include low dose aspirin, propranolol, tricyclic antidepressants such as amitriptyline, and calcium channel antagonists. These should be used in a stepwise fashion, with aspirin being the first line as this poses least risk to mother and fetus [1].

Secondary headaches

Secondary headaches are headaches caused by an underlying medical condition. These conditions can be benign (e.g. Idiopathic Intracranial Hypertension) or can be the first sign of serious underlying pathology (e.g. CVT). Therefore it is important to know how to differentiate and investigate these headaches appropriately in order to reduce morbidity.

Hypertension/ Pre-Eclampsia

Hypertension in pregnancy falls under the following classifications in the NICE guidelines, depending on the onset of the hypertension and whether significant proteinuria is present or not:

- Chronic Hypertension – hypertension present prior to conception
- Gestational Hypertension – new onset hypertension after 20 weeks gestation
- Pre-Eclampsia – new onset hypertension after 20 weeks gestation with significant proteinuria [10]

Headache is a common presenting feature of hypertension. The most worrying underlying conditions are uncontrolled hypertension and Pre-Eclampsia, as complications can include eclamptic seizures and stroke [11]. The features of a headache secondary to hypertensive

disorders are as follows:

- Bilateral
- Pulsating
- Aggravated by physical activity [3,5]

Pre-eclampsia is defined as pregnancy induced hypertension (BP >140/90 mm Hg) with associated proteinuria (>0.3g in 24 hours). In pre-eclampsia, patients may complain of severe frontal headaches, visual disturbances, epigastric pain most importantly sudden swelling (oedema) of face, hands and feet [11].

Neurological examination of a patient with pre-eclampsia underlying a headache may have brisk reflexes with clonus. There should not be any focal neurology present. Investigation of any pregnant woman presenting with a headache should include a blood pressure reading and urine dip in order to rule out pre-eclampsia.

Idiopathic intracranial hypertension

Idiopathic intracranial hypertension (IIH) is a benign condition characterised by increased pressure of the Cerebrospinal Fluid (CSF) (>250 mm H₂O at lumbar puncture) without any features of space occupying lesion or hydrocephalus [12]. The underlying pathophysiology is unknown, but it is known to be 8 times more common in women than in men and in obese patients in the childbearing years [5,12]. The headache associated with IIH has the following features:

- Diffuse constant pain
- Aggravated by coughing or straining
- Often retro-orbital, but can be in close temporal relation to the area of increased pressure [1,3]

Neurological examination will reveal no focal neurology, although papilloedema is observed and occasionally unilateral or bilateral sixth nerve palsy can be seen. The patient may complain of visual disturbances, including visual field defect and reduced visual acuity [1,12].

IIH is a diagnosis of exclusion and should be fully investigated to rule out other differential diagnoses, including space occupying lesions and CVT [12]. A CT scan of the head will rule out any space occupying lesions, whilst an MRI with contrast will rule out a CVT. IIH is not a risk to the pregnancy and any decisions regarding mode of delivery should be made based on obstetric factors only [12]. A lumbar puncture can be performed safely in pregnancy, and examination of the CSF will show a normal composition. Studies have shown that pregnancy does not have any impact on the composition of the CSF, therefore if there are abnormalities discovered they should be taken seriously [6].

Management of IIH is the same during pregnancy and in the non-gravid patient. Lifestyle modifications like weight reduction and optimising weight control during pregnancy is first line. Ophthalmological review of visual fields looking specifically for progressive changes is a marker of severity. Urgent intervention is required where visual symptoms are found. Medical management includes appropriate use of analgesia and carbonic anhydrase inhibitor i.e. acetazolamide [1,12]. This medication is best avoided in the first trimester [1]. Excessive CSF production may be an indication for repeated lumbar puncture or more permanent measures such as lumboperitoneal or ventriculoperitoneal shunts [12].

Subarachnoid haemorrhage

Subarachnoid Haemorrhage (SAH) following a ruptured

intracranial aneurysm is a rare but potentially serious complication of pregnancy. Physiological changes during pregnancy can predispose to an increased risk of SAH, particularly during the third trimester when maternal cardiac output and circulating volume reaches its maximum. In addition, it is also thought that increased exposure to circulating hormones including oestrogen, progesterone and human chorionic gonadotrophin may predispose to development or progression of intracranial aneurysms [13].

The incidence of SAH during pregnancy and puerperium is within the range of 3 to 10 per 100,000 pregnancies [14]. A typical presentation would involve a sudden onset 'thunder clap headache' described as the 'most severe headache', often of a short lived duration. Other symptoms can include neck stiffness, photosensitivity, diplopia, seizures or fluctuating consciousness. Symptoms preceding the headache involving a third nerve palsy associated with retro-orbital pain and mydriasis may herald an impending rupture of a posterior communicating artery aneurysm. Neuroradiological imaging in the form of CT is the imaging modality of choice. If the diagnosis remains in doubt, a lumbar puncture could be performed in the absence of contraindications to investigate for the presence of xanthochromia, which is diagnostic. Management of ruptured intracranial aneurysms during pregnancy are largely based on careful considerations given to maternal health at presentation, gestational age of the pregnancy and neurosurgical opinion. Emergency caesarean section followed by neurosurgical intervention [clipping or coiling of aneurysm] could be indicated following a positive diagnosis. Although SAH during pregnancy may be associated with high morbidity and mortality, the necessity of intracranial screening for high-risk pregnancies remain controversial [14].

Cerebral venous thrombosis

Physiological changes to the coagulation system during pregnancy and puerperium render the maternal circulation a prothrombotic state and therefore at an increased risk of thrombus formation and stroke. Some of these physiological adaptations include a reduction in protein S levels and an overall increase in levels of coagulant factors V, VIII, IX, X and fibrinogen thus creating an overall shift towards a hyper-coagulable state. This is thought to be in anticipation of the haemostatic challenges of delivery and tends to persist during puerperium. In addition, prolonged bed rest, instrumental delivery or caesarean section are amongst the other well recognised factors predisposing to tendencies towards thrombosis secondary to venous stasis and hypercoagulability [15,16].

Among the potentially life threatening causes of secondary headaches, Cerebral Venous Thrombosis (CVT) accounts for a large proportion of the cases accounting for an incidence estimated at 11.6 per 100,000 deliveries [17]. The condition is most commonly encountered either late in pregnancy (women in their third trimester of their pregnancy) or postpartum, with these women being at greatest risk. However, cases have been reported as early as 8 weeks [16]. The clinical manifestations of obstetric CVT appear relatively similar to CVT unrelated to pregnancy with headache being the most commonly reported initial symptom. Lurlaro et al in their prospective multi centric study noted several characteristic features of headache in CVT including a tendency towards an acute/sub-acute onset, moderate to severe pain, localized and continuous symptom [18]. Other symptoms include focal deficits, seizures and altered mental status especially drowsiness and somnolence have also been noted. Cantu et al in their review also reported the tendency towards a more acute course with early stabilization observed among patients with obstetric related CVT [19].

The imaging modality of choice for patients with headache suspicious of CVT is Magnetic Resonance Imaging (MRI) with T2 weighted imaging and MR venography. However, due to lower cost and ready availability, CT is widely used as the initial imaging modality. CT has relatively low sensitivity however, with detection rates of only 30% [5]. In addition, further investigations may be necessary if underlying thrombophilia, inflammatory or vasculitic disorders were suspected.

Treatment of CVT consists of anticoagulation with low molecular weight heparin of at least six months duration to prevent further thrombosis. Endovascular therapy can be considered in cases of neurological deterioration in spite of anticoagulation.

Owing to recent advancements in neuro-radiological imaging, which has enabled both early diagnosis and management, a trend towards lower mortality rates as well as improved outcomes have increasingly been observed. Previous studies of various obstetric CVT series have reported mortality rates ranging from 4-33% [16,20,21]. The long term outcome including likelihood of recurrence of CVT during subsequent pregnancies remains unclear. However, it is known that these patients are at a higher risk of further thrombotic events and hence recommendations for prophylactic LMWH during pregnancy and the puerperium [5].

Reversible cerebral vasoconstriction syndrome

Reversible Cerebral Vasoconstriction Syndrome (RCVS) is among the other secondary headache disorders that are increasingly recognised with significant associations with the puerperium [22]. Other known precipitating factors include the use of vasoconstrictive medications, with ergot derivatives mainly implicated [23]. RCVS is a form of post-partum angiopathy characterised by angiographic appearance of multifocal arterial constriction and dilatation. Headache is the most commonly reported symptom and is often seen in association with other symptoms, including altered mental state (confusion, agitation), visual disturbances (blurring of vision and photophobia), seizures, nausea and vomiting [22]. Unlike other secondary headache disorders, the headache in RCVS can be distinguished mainly by its characteristic diffuse, sudden and severe onset occurring in multiple attacks, not infrequently described as a 'recurrent thunderclap headache' [22].

Diagnosis is confirmed by demonstration of characteristic 'string of beads' appearance on angiography typically with spontaneous resolution of symptoms within 1-3 months [5]. Given the overlapping presentations of postpartum angiopathy and various other secondary

headache disorders, relevant investigations to exclude a diagnosis of subarachnoid haemorrhage and eclampsia also form part of the diagnostic workup. Careful considerations of some of the accompanying features can be useful, including BP and proteinuria, which are of particular significance.

At present, there are no known treatments for RCVS. Treatments including calcium channel antagonists, magnesium sulphate and high dose corticosteroids have been trialled with good outcomes [22,24].

Assessment of headaches in pregnancy

In most cases, pregnant women with primary headache disorders have been diagnosed before pregnancy. However, as many as 10% present initially or are first diagnosed during pregnancy [25]. In addition, obstetric complications giving rise to secondary headaches or headache disorders presenting only during pregnancy may also occur.

A detailed account of the timeline of the headache and its relation to the current pregnancy or any previous pregnancies should therefore be accurately established (Box 1). Other features within the headache history including the severity, frequency of attacks, location, character of the pain and any associated symptoms considered as appropriate. A high index of clinical suspicion of a serious secondary cause of headache in women who present with certain 'red flag' features should be maintained (Box 2) [26,27].

A thorough neurological examination should follow in order to evaluate key symptomatology elicited from the history. Key examinations used to evaluate headache in pregnancy and puerperium include the following [5]:

- Fundoscopy for signs of raised intracranial pressure e.g. papilloedema
- Full neurological examination: tone, power, reflexes and coordination of all four limbs
- Plantar responses
- Cranial nerve assessment
- Gait assessment
- Blood pressure, urinalysis for proteinuria and clonus

The approach to neuro-radiological imaging in pregnancy is largely guided by desires to avoid potentially harmful foetal exposures to

- Establish timeline – duration, frequency of attack; onset and relationship to current and previous pregnancies
- Location – unilateral vs bilateral
- Character – type of pain: 'pressure' vs 'tightness' vs 'pulsating'
- Associated symptoms- aura, nausea, vomiting, visual disturbances (scotoma, photophobia), neurological symptoms (new onset seizures, weakness, sensory or motor deficit, dysphasia, ataxia)
- Relevant medical/ surgical/ psychiatric history which may exacerbate or complicate headache
 - Risk factors for pregnancy related stroke – DM, pre-existing hypertension or hypertensive disorders of pregnancy, migraine with aura, sickle cell disease
 - Risk factors for thrombophilia
 - Depressive disorder
- Medication history – substance misuse, vitamins, herbal remedies, sinus medications, caffeine intake

BOX 1: Key features to obtain in the history when assessing headaches in pregnancy.

'Red flag' signs and symptoms	Differential diagnosis
Thunderclap: rapid duration from onset to peak headache intensity (seconds to minutes) -	<ul style="list-style-type: none"> • Subarachnoid haemorrhage • Postpartum angiopathy • Pituitary apoplexy
Focal neurological symptoms e.g. limb weakness, aura <5min or >1hour	<ul style="list-style-type: none"> • Migraine • Stroke or TIA
Non-focal neurological symptoms e.g. cognitive disturbances	<ul style="list-style-type: none"> • Cerebral venous thrombosis
Change in frequency, characteristics of headache or its associated symptoms	
Abnormalities in neurological examination	
Headache associated with postural changes	
Headache upon waking up	<ul style="list-style-type: none"> • Raised intracranial pressure (space occupying lesion, idiopathic intracranial hypertension) • Migraines
Headache precipitated by physical exertion or Valsalva manoeuvre	<ul style="list-style-type: none"> • Raised intracranial pressure • SAH
Patients with risk factors for cerebral venous sinus thrombosis	<ul style="list-style-type: none"> • Known coagulopathy • Recent immobility
Jaw claudication or visual disturbances	<ul style="list-style-type: none"> • Temporal arteritis
Fever	<ul style="list-style-type: none"> • Intracranial or systemic infection
Neck stiffness (meningeal irritation)	<ul style="list-style-type: none"> • Meningitis
New onset of headache in an immunocompromised patient	<ul style="list-style-type: none"> • HIV infection
New onset of headache in a patient with known history of malignancy	

BOX 2: Red flag features suggestive of serious underlying disorder requiring further investigations

radiation and contrast material. In clinical practice however, the choice of imaging modality is still much guided by the suspected pathology and availability of radiological services. During pregnancy, 50mGy is generally taken as the cut off for accepted background cumulative dose of ionising radiation. Foetal radiation exposure through scatter appears to be minimal during maternal head CT, estimated at <0.005mGy. MRI appears to be preferential to any other imaging modality involving ionizing radiation however should be avoided in the first trimester due to potential hazards of hyperthermia and acoustic noise [5]. Current recommendations are that iodinated contrast materials to be used in pregnancy only where clinically indicated. Evidence suggests that the iodinated contrast materials cross the placenta to produce transient effects on the developing foetal thyroid gland and, hence, if used in pregnancy, foetal thyroid function should be evaluated on delivery. Gadolinium based contrast agents have an overall better safety profile during pregnancy [28,29]. Lactating women can continue to breast feed as concentrations of iodinated or gadolinium based contrast within breast milk are negligible [28].

Conclusion

Headaches in pregnancy and the puerperium is not an uncommon occurrence, accounting for a considerable proportion of avoidable morbidity and mortality. Although primary headache disorders account for most cases, a high clinical suspicion for secondary headaches is necessary to avoid delayed diagnosis of headaches secondary to obstetric complications or conditions. The management of headaches

during pregnancy appears to be relatively similar to that outside of pregnancy. However, careful considerations have to be made including plans for delivery, safety of medication use antenatally and when breast feeding as to optimize management and overall outcomes of pregnancy.

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