Postpartum Headache: A Prospective Study

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Aims: To prospectively assess the incidence and etiology (ie, primary vs symptomatic) of headache in women during the first month postdelivery, with particular emphasis on the type of presentation as a clue for identifying potentially harmful etiologies. A secondary aim was to evaluate the relative frequency of migraine- vs tension-type headache in cases of primary headache. **Methods:** A total of 900 consecutive women were enrolled in the study and examined within 3 days of delivery, both clinically and with transcranial color-coded sonography (TCCS). During the course of follow-up, all subjects presenting with headache suspected of being secondary to intracranial pathology underwent a complete clinical and instrumental assessment with TCCS and magnetic resonance imaging (MRI) and angiography. A telephone interview was administered to all subjects 1 month after delivery. Two-tailed *t* test, Mann-Whitney test, Pearson chi-square test, and multiple logistic regression were used to analyze the data. **Results:** At the end of the follow-up period, 241 women (26.8% of the sample) reported at least one headache attack. In 88 of these 241 cases (9.8%), the headache attack occurred soon after delivery and was already recorded at the first visit. Thunderclap headache occurred in 34 (3.8%) of the subjects. In all but one of these subjects, the course was spontaneously benign. None of the recorded variables allowed discrimination of the subjects with thunderclap headache from those without headache. Three subjects had thunderclap headache following dural anesthesia, and one subject was found to have reversible cerebral vasoconstriction syndrome. Headache with gradual onset was recorded in 207 subjects (23%). Three of these subjects fulfilled the criteria for pre-eclampsia, and 13 had postural headache after dural anesthesia. Migraine history and urinary protein were independent predictors of gradual onset headache, and migraine history and parity were significant independent predictors of pulsating pain with gradual onset headache. **Conclusion:** Headache appeared early in the first days postdelivery, and its incidence increased in the first month thereafter. Predictors were different according to whether the headache had a gradual onset or a thunderclap presentation. Primary headache accounted for the overwhelming majority of the recorded cases. *J Oral Facial Pain Headache 2017;31:346–352. doi: 10.11607/ofph.1869*

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Puerperium can put women at a particularly high risk of suffering a number of different cerebrovascular insults.[1–5] Headache precedes the occurrence of more severe signs and symptoms in many of these insults and therefore represents a warning signal,[6] but headache is also one of the most commonly reported complaints in the first month postpartum.[7–9] Primary headache has accounted for the vast majority of reports in previously published case series, but the retrospective nature of the collected cases or selection bias favoring inclusion of migraineurs limits the validity of this data.[10,11]

The type of headache presentation may hint at the possible underlying pathophysiologic mechanisms. Acute onset headaches peaking in less than 1 minute, otherwise known as thunderclap headache, are typically indicative of subarachnoid hemorrhage, but may also be related to reversible cerebral vasoconstriction syndrome (RCVS), for

which puerperium is an acknowledged precipitating factor.[12–17] Furthermore, thunderclap presentation of headache is reported in 2% to 10% of patients with cerebral venous sinus thrombosis, 20% of patients with cervical artery dissection, and at lower frequencies in ischemic stroke, retroclival hematoma, pituitary apoplexy, and third-ventricle colloid cyst.[18] Primary thunderclap headache with no associated brain abnormality has become recognized as a clinical entity as well, although this is a last-resort diagnosis after all possible alternative causes have been ruled out with an appropriate diagnostic work-up.[12,18,19]

The present study was undertaken with the primary aim of prospectively assessing the incidence and etiology (ie, primary vs symptomatic) of headache in women during the first month postdelivery, with particular emphasis on the type of presentation as a clue for identifying potentially harmful etiologies. A secondary aim of the study was to evaluate the relative frequency of migraine- vs tension-type headache in cases of primary headache.

Materials and Methods

The study protocol was approved by the S. Orsola Hospital Institutional Review Board. All patients provided informed consent before entering the study. They were recruited patients who had given birth in the Obstetrics Department of the S. Orsola Hospital (ie, the first 86 cases were recruited here, then from Poliambulanza Hospital, as the former was incorporated in the latter) in Brescia, Italy. The subjects underwent a first visit within 96 hours of delivery, during which a chart review was performed and a structured interview with particular emphasis on headache administered in person by one research assistant. The following data were collected: age, ethnicity, height, weight gain, arterial blood pressure (ABP), history of primary headache disorders, history of arterial hypertension, smoking habits, alcohol intake, diabetes, dyslipidemia, family history of stroke, and detailed characteristics of recent pregnancy and delivery, including anesthesia, medications, and drugs taken during pregnancy. Hemoglobin, uric acid, and urinary protein levels were also recorded in all subjects. Thereafter, ABP was measured noninvasively, and a transcranial ultrasound study was performed in all subjects. A brief neurologic examination was performed in subjects complaining of headache to exclude signs suggestive of focal deficit, intracranial hypertension, or meningeal irritation.

Headache intensity was evaluated by using a visual analog scale (VAS) ranging from 0 (no pain) to 10 (worst pain imaginable). Headache attacks reaching a maximum intensity of above 7 in less than 1 minute were qualified as thunderclap headache, and those peaking more slowly were classified as gradual onset headache. Headache pain was systematically classified whenever possible as pulsating, pressing/tightening, or neuralgic (like a sudden shock of electricity). Headache reported in the medical history was classified according to the 2013 criteria of the International Headache Society.[12]

A baseline assessment with transcranial color-coded sonography (TCCS) was performed in all subjects to detect any early sign of vasospasm. The M1 and M2 segments of the middle cerebral artery (MCA) were identified, and mean flow velocity (MFV) was recorded.[20] An MFV of 100 cm/second was selected as the normal upper limit in this study.[21] In subjects with an MFV exceeding the threshold, the Lindegaard Index (LI) was calculated by dividing the MFV in the MCA by the MFV of the ipsilateral distal extracranial internal carotid artery (ICA). Published studies have indicated that an LI of 3 to 6 can be considered as mild vasospasm, and greater than 6 a moderate to severe vasospasm.[22]

All subjects were further instructed to pay special attention to the occurrence of sudden thunderclap headache in the following month and in such a case to access the Emergency Ward of the Hospital for expedited assessment or to contact by phone one of the study researchers. For the assessment of subjects with headache suspected of being secondary to intracranial pathology, the protocol included a full neurologic examination, TCCS, magnetic resonance imaging (MRI), and magnetic resonance angiography (MRA).

To ensure complete collection of information, all subjects were reassessed at 1 month after hospital discharge by a structured telephone interview inquiring about the occurrence and detailed characteristics of any type of headache, focal neurologic deficits, and/or seizures since delivery. Subjects answering positively were invited to a neurologic examination.

Continuous variables were expressed as mean ± standard deviation (SD) and compared by means of two-tailed *t* test if normally distributed or with Mann-Whitney test if the distribution was not normal. Frequencies were compared with Pearson chi-square test. Multiple logistic regression was used to assess predictors of headache. The SPSS program (version 22) was used. A P value of $< .05$ was considered significant.

Results

A total of 1,000 subjects were screened during the inclusion period of 20 months. Of these subjects, 35 refused to participate, 10 were unsuitable for TCCS, 30 were unavailable for follow-up, and for

Table 1 Demographic, Anthropometric, and Biologic Variables

Variables	n	Available cohort	Mean ± SD	%
Categorical				
History of migraine	292	850		34.4
History of tension-type headache	164	850		19.3
History of hypertension	35	863		4.1
History of diabetes	39	869		4.5
Hystory of dyslipidaemia	30	850		3.5
Active smoking	145	900		16.1
Alcohol (≥ 2 drinks/d)	9	900		1.0
Ergot during delivery	500	900		55.6
Continuous				
BMI		892	22 ± 4	
Gestational age (wk)		892	39 ± 2	
Systolic BP (Hg/mm)		829	110 ± 12	
Diastolic BP (Hg/mm)		829	68 ± 9	
Urinary protein (mg/dl)		769	7.8 ± 19.6	
Hb (g/lt)		758	11.3 ± 1.3	

SD = standard deviation; BMI = body mass index; BP = blood pressure; Hb = hemoglobin.

25, linguistic incompetence made the collection of meaningful data impossible. Thus, 900 women were enrolled in the study. Mean age was 31 ± 5 years (range 16 to 45), 75% were of Caucasian ethnicity, and 477 (53%) were experiencing their first pregnancy, 288 (32%) their second pregnancy, and the remaining 135 (15%) their third to sixth pregnancies. The subjects were evaluated at a mean of 1.5 ± 1 days postpartum (range 0 to 11), and the follow-up telephone interview occurred at a mean of 39 ± 11 days (range 25 to 50) after childbirth. A past history of headache was available in 850 subjects: 292 (34.4%) reported past migraine, and 164 (19.3%) reported past tension-type headache. Further demographic and biologic findings are presented in Table 1.

At the end of the follow-up period, 241 women (26.8%) reported at least one headache attack. In 88 of these 241 cases (9.8%), the headache attack occurred soon after delivery and was already recorded at the first visit.

In 16 of the 283 women who had undergone spinal anesthesia during delivery, postural worsening of headache was attributed to intracranial hypotension. Three subjects with headache at the first visit fulfilled the criteria for pre-eclampsia (ie, proteinuria and hypertension at the end of pregnancy). One subject was admitted to the hospital for recurrent thunderclap headache during the follow-up, and RCVS was diagnosed.[19] Eight further subjects contacted the research staff for a single episode of thunderclap headache during the follow-up period. They were all examined as per the protocol (clinical assessment, MRI, and MRA), but tested negative for RCVS. Therefore, a total of 20 out of 241 cases of headache could be attributed to a specific cause (Tables 2 to 4).

Headache presented as thunderclap in 34 subjects and as gradual onset in the remaining 207. Median intensity of thunderclap headache pain was 7 on the VAS, and for headache with gradual onset the median intensity of pain was 5 ($P < .0001$). Pain was pulsating or neuralgic in 25 of 34 cases (73.5%) of thunderclap presentation and pressing/tightening in the remaining 9 (26.5%). When onset was gradual, pain was reported as pulsating or neuralgic in 87 of 207 subjects (42%) and pressing/tightening in the remaining 120 (58%); This difference was statistically significant ($P < .0001$).

Thunderclap presentation was more often symptomatic than gradual onset headache, since it was associated with RCVS in one case and with intracranial hypotension in three cases (11.7%). In the 207 women with gradual onset headache, a specific cause was detected in only 16 instances (7.7%; 13 postdural anesthesia and 3 as a consequence of pre-eclampsia).

Of the overall sample of 900 subjects, intracranial MFV tended to be higher in subjects with headache compared to those without headache (respectively: right M1 = 77 + 19 vs 73 + 17; right M2 = 74 + 19 vs 73 + 17; left M2 = 76 + 23 vs 72 + 17), but only for the left M1 (78 + 20 vs 73 + 17) was the difference barely significant ($P = .047$).

Univariate analyses were conducted separately for subjects with gradual onset or thunderclap headache in comparison with subjects who had not had headache during the follow-up. None of the variables assessed at the first visit differentiated subjects with thunderclap headache from those without headache, whereas history of migraine was significantly more frequent and urinary protein levels significantly higher in subjects with gradual onset headache (Table 2). Parity (the number of times a woman has carried a pregnancy to a viable gestational age) showed a nonsignificant trend for a protective effect: the higher the parity, the lower the likelihood for gradual onset headache (26.2% on average until third pregnancy vs 16.4% from the fourth pregnancy onward).

Multiple regression analysis revealed no independent predictor of thunderclap headache, whereas past migraine and urinary protein were independent predictors of gradual onset headache (Tables 5 and 6). Indeed, compared to subjects without urinary protein and without history of migraine, those who had both conditions developed postpartum headache in 40% vs 18.1% of cases ($P < .0001$).

In subjects with gradual onset headache, a further analysis was performed.

Table 2 Comparison of Variables Between Subjects With Thunderclap (TH) or Gradual Onset Headache (GOH) and Subjects Without Headache (NH) at the 1-Month Follow-up

	No headache (n = 659)	Thunderclap headache (n = 34)	Gradual onset headache (n = 207)	*P* value
Continuous variables (mean ± SD)				
BMI	23 ± 4	23 ± 4	23 ± 4	NS
Age (y)	31 ± 5	30 ± 6	31 ± 2	NS
Weight gain (kg)	13 ± 5	12 ± 4	13 ± 4	NS
MFV: Right M1 (cm/s)	74 ± 17	75 ± 15	74 ± 20	NS
MFV: Right M2 (cm/s)	72 ± 17	75 ± 20	74 ± 18	NS
MFV: Left M1 (cm/s)	73 ± 17	78 ± 17	75 ± 20	NS
MFV: Left M2 (cm/s)	72 ± 17	76 ± 18	75 ± 18	NS
Systolic BP (Hg/mm)	111 ± 12	112 ± 12	112 ± 14	NS
Diastolic BP (Hg/mm)	68 ± 9	70 ± 8	71 ± 9	NS
HB (g/lt)	11.3 ± 1.3	11.3 ± 1	11.4 ± 1.5	NS
Urinary protein (mg/dl)	6.8 ± 13	6.0 ± 9	11.7 ± 34	.001[a]
Categorical variables (%)				
History of migraine	29.9	30.3	48.5	< .0001[a]
Present or past eclampsia	4	2.9	3.9	NS
Spinal anesthesia	15.5	14.7	11.7	NS
Methylergonovine during delivery	60.5	51.7	58.5	NS

NS = not significant. MFV = mean flow velocity; M1 and M2 = segments of middle cerebral artery; HB = hemoglobin. [a]Significant comparison between no headache and gradual onset headache.

Those who reported pulsating pain had a significantly more frequent history of migraine (61.4% vs 39.4%, $P = .003$) and were less likely to be experiencing their first pregnancy (33% vs 66.7%, $P = .04$) compared to those with pressing/tightening pain. Both history of migraine and parity remained independent predictors after regression analysis, but in addition, the use of methylergonovine during labor also became a significant independent predictor of pulsating headache (Table 7).

Table 3 Headache Incidence, Etiology, and Risk Factors as Assessed at 30 Days Follow-up (N = 900)

Etiology	n	%	Risk factors
Primary headache			
Unspecified	221	24.6	Past migraine, urinary protein
Symptomatic headache			
Pre-eclampsia	3	0.3	Urinary protein, hypertension
RCVS	1	0.1	None identified
Intracranial hypotension	16	1.8	Lumbar puncture
Total	241	26.8	

RCVS = reversible cerebral vasoconstriction syndrome.

Table 4 Distribution of Headache According to Presentation, Clinical Features, and Etiology

	Headache pain, n (%)		Etiology, n (%)	
Presentation	Pulsating	Pressing/ tightening	Symptomatic	Primary
Thunderclap (n = 34)	25 (73.5)	9 (26.5)	4 (11.7)	30 (88.3)
Gradual onset (n = 207)	87 (42)	120 (58)	16 (7.7)	191 (92.3)
Total (n = 241)	112 (46.5)	129 (53.5)	20 (8.3)	221 (91.7)

Discussion

The present study was undertaken primarily to establish the incidence of puerperal headache with the secondary aim of assessing to what extent the type of presentation and clinical features contribute to the differentiation of primary from symptomatic headache. Early postdelivery headache was detected in 88 women (9.8% of the entire cohort) at the first visit. All 16 cases of postural headache and the 3 cases of headache associated with pre-eclampsia were identified at this stage.

By the end of the follow-up, the number of subjects who had headache rose to 241 (26.8% of the entire cohort). Of these, 34 had a thunderclap presentation. One of these subjects developed RCVS, but in the remaining 33 the course was benign with spontaneous remission and no clinically suspicious signs or symptoms. Eight of these 33 patients were examined, and clinical, neurosonologic, and neuroradiologic assessment did not reveal any structural abnormalities. Pain in these subjects was severe (median of 7 on a VAS) and pulsating in the majority of cases. Neither univariate nor regression analyses identified any meaningful risk factor. There is the question of whether these 33 cases represent true examples of primary headache or minor manifestations of benign vasospastic syndrome, but since not all cases were assessed with angiography at the appropriate time, this question cannot be answered, and it is

Table 5 Multiple Regression Analysis with Thunderclap Headache as Dependent Variable

			95% CI	
	Sig	OR	Lower	Upper
History of migraine	.954	0.971	0.366	2.579
Urinary protein	.574	0.987	0.942	1.034
Parity	.352	1.236	0.791	1.931
Mean arterial pressure	.467	1.017	0.972	1.065
Age	.546	0.973	0.892	1.062
Type of delivery	.924	0.973	0.550	1.719
Methylergonovine	.084	2.285	0.894	5.838

Sig = significance; OR = odds ratio; CI = confidence interval.

Table 6 Multiple Regression Analysis with Gradual Onset Headache as Dependent Variable

			95% CI	
	Sig	OR	Lower	Upper
History of migraine	.000	0.446	0.298	0.667
Urinary protein	.020	0.989	0.979	0.998
Parity	.061	1.276	0.989	1.645
Mean arterial pressure	.193	1.015	0.993	1.038
Age	.186	0.972	0.932	1.014
Type of delivery	.474	1.114	0.829	1.497
Methylergonovine	.737	0.929	0.602	1.432

Sig = significance; OR = odds ratio; CI = confidence interval.

Table 7 Multiple Regression Analysis with Pulsating Pain in Gradual Onset Headache as Dependent Variable

			95% CI	
	Sig	OR	Lower	Upper
History of migraine	.001	3.774	1.672	8.521
Urinary protein	.433	0.994	0.981	1.008
Parity	.023	2.690	1.144	6.326
Mean arterial pressure	.955	1.001	0.957	1.048
Age	.422	0.964	0.880	1.055
Type of delivery	.051	1.885	0.998	3.560
Methylergonovine	.006	0.282	0.114	0.696

Sig = significance; OR = odds ratio; CI = confidence interval.

therefore possible that some cases of benign RCVS were missed. Whatever the cause, however, the clinical course was benign, and the headache subsided without any residual deficit, which alone rules out other potentially dangerous etiologies.[18] Of note is the finding that neither history of migraine nor the use of methylergonovine during delivery played any role in facilitating or predicting thunderclap presentation.

In contrast, in the 207 subjects with gradual onset headache, median pain severity was moderate (median of 5 on the VAS) and history of migraine a significant predictor, confirming data from the literature.[23,24] Furthermore, history of migraine was significantly more frequent in subjects with pulsating pain than in those with pressing/tightening pain. In a further regression analysis, migraine history, parity, and use of methylergonovine were significant predictors of pulsating pain in subjects who complained of gradual onset headache.

MFV in the MCA in subjects who reported headache at final follow-up tended to be higher than in headache-free subjects. It may be hypothesized that increased blood loss, which is known to affect MFV in brain vessels, might have enhanced the appearance of headache in susceptible patients,[25,26] although no specific explanatory analysis was performed.

Urinary protein at the end of pregnancy was significantly higher in subjects with gradual onset headache compared with headache-free subjects. Urinary protein was an independent predictor of gradual onset headache following regression analysis, but did not discriminate pulsating from pressing/tightening headache. It may be speculated that urinary protein, which was recorded in 241 subjects in significant amounts (> 10 mg/dL), might represent a marker of minor endothelial dysfunction related to terminal pregnancy even in the absence of overt signs of pre-eclampsia.[27,28] Migraine has also been linked to endothelial dysfunction, although the evidence is controversial,[29,30] and is recognized as a risk factor for pre-eclampsia.[31] It is thus possible that in subjects with significant urinary protein, minor endothelial dysfunction may have lowered the threshold for developing headache. Indeed, 40% of subjects with both urinary protein and history of migraine developed postpartum headache compared to 18.1% of those who had neither.

Univariate analysis showed that parity had a nonsignificant protective effect, since women with a parity > 3 tended to complain less frequently of headache. In addition to migraine history and use of methylergonovine, parity was significant in predicting pulsating pain when headache had a gradual onset; ie, the higher the parity, the less the likelihood of getting headache as a whole, but when headache did occur, it was more often pulsating. This suggests that women with more past pregnancies were less likely to develop headache as a response to the anxiety/stress generated by parturition and were probably more likely to experience the resurgence of migraine than women in their first pregnancies, in whom tension-type headache was predominant. Admittedly, the identification of pulsating headache with migraine is an oversimplification, as other features of migrainous pain (eg, nausea, phono- or photophobia, and strain exacerbation) were not systematically assessed.

In contrast to the present findings, parity has been reported to be associated with an increased risk of headache.[7,24] The different timing of data collection, which was within a mean of 7 days postchild-

birth in both earlier studies, may partly explain the discrepancy with the present findings.

The administration of methylergonovine during delivery had no apparent effect on subsequent headache appearance, but it predicted pulsating pain in subjects with gradual onset headache. Headache is included among the untoward effects of methylergonovine,[32] and it is possible that the known effect of the drug on vascular tone may explain this finding.

Overall, the present findings were consistent with the literature in demonstrating that headache is a very early complaint in about 10% of women who have just given birth, but contrary to other studies,[7,8] the incidence of headache rose to about 27% in the month after childbirth. Overall, this figure is in the range of previous reports of an incidence of 11% to 39%,[7] but lower compared with that found in the only study that examined patients in the early postpartum period[7] (38.7%). However, this could be because in the earlier study the assessment was performed on average 7 days postpartum, whereas in the present study it took place at a mean of 1.5 days after childbirth.

Postpartum headache has a number of possible etiologies,[6,33] but most often occurs without demonstrable brain pathology, hence the definition of primary headache. In a prospective series of 985 women interviewed at a mean of 7 days after delivery, Goldszmidt et al[7] found that tension-type headache alone accounted for 38.3% of all reported headaches, followed by migraine (overall 34.1%) and other ill-defined primary headaches, the only secondary cases being referred to postdural puncture (overall 4.7% of cases). On the other hand, Stella et al,[8] although confirming tension-type headache as the most frequent postpartum headache (39%), found that headache was secondary to a brain disease in 50% of cases (pre-eclampsia in 24%, postdural puncture in 16%, pituitary pathology in 3%, cerebral venous thrombosis in 3%, cerebral vasculopathy in 2%, thalamic lesion in 1%, and subarachnoid hemorrhage in 1%) in 95 hospitalized patients. Clearly, a selection bias favoring the most severe or suspicious cases of headache explains the different distribution between primary and secondary headache types.

In the present study, special emphasis was placed on headache presentation as a basic clue for diagnosis by separating headaches with sudden and gradual onset. However, with the only exception being the one case of RCVS, which was suspected based on clinical presentation, gradual and thunderclap onsets were almost equally represented in primary and symptomatic headaches. The overwhelming majority of recorded cases overall were attributable to primary headache, as there was only 1 case of RCVS, 3 cases of headache associated with pre-eclampsia, and 16 cases in whom headache resulted from postdural puncture.

TCCS, which was employed as a screening tool to detect early vasoconstriction of cerebral vessels, proved useful for detecting the single case of RCVS, but threshold criteria different from those suggested in the literature had to be set due to the particular hemodynamic state of the examined subjects.[19,34] Further details on this subject are to be found in a separate report.[35]

Strengths of the present study were its prospective nature, the large cohort size, the systematic investigation of all included cases, and follow-up with no loss of participants, which allowed the complete collection of information. The main limitation of this study was that it was based on the experience of a single center. A further limitation was the use of TCSS instead of MRA to screen for possible RCVS.

Conclusions

The present findings suggest that primary headache accounts for the majority of cases of headache occurring during puerperium. The onset is most often gradual. The pain is either pulsating or pressing/tightening at approximately the same frequency and may also have an explosive presentation in a nonnegligible minority of subjects. Predictors differ according to whether the presentation is thunderclap or gradual. Thunderclap headache presentation appears to entail an overall benign prognosis, but timely and appropriate investigations are needed to identify those cases in which the underlying mechanism resides in vasoconstriction of cerebral vessels.[36]

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