

Comorbidity of Major Depression and Migraine— A Canadian Population-Based Study

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Objective: To estimate the prevalence of major depressive episodes (MDEs) in patients with migraine and to compare the strength of association with that of other long-term medical conditions.

Methods: This study used a large-scale probability sample (over 130 000 sample) from the Canadian Community Health Survey (CCHS), a cross-sectional survey conducted by Statistics Canada. The CCHS screened for a broad set of medical conditions. Major depression was evaluated with the Composite International Diagnostic Interview Short Form for Major Depression, and the diagnosis of migraine was self-reported. The annual prevalence of major depression was calculated in the general population, in subjects with migraine, and in those with chronic conditions other than migraine.

Results: The prevalence of major depression in subjects reporting migraine was higher than that in the general population or in subjects with other chronic medical conditions (17.6%, compared with 7.4% and 7.8%, respectively).

Conclusions: There is a strong association between major depression and migraine. The migraine–MDE association may account for a large fraction of the chronic condition–MDE association. The association between migraines and MDE differs from that of other chronic conditions, as the association persists into older age groups.

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Clinical Implications

- Because of the high participation rate and sampling procedure, the results reported here can be interpreted as representative of the entire Canadian population and are less susceptible to the bias of studies of clinical samples.
- This information is essential for planning health services and prioritizing further research in this area.
- It is important for both psychiatrists and health care clinicians in routine clinical setting to be aware of the high, increased risk of MDE associated with migraine in all age groups.
- Clinicians are challenged to recognize that MDE and migraine coexist and to take this coexistence into account when developing treatment strategies. Possibly, more patients could benefit from a multidisciplinary intervention.

Limitations

- The presence of migraine was self-reported and not diagnosed. Some patients suffering from chronic headaches might have been diagnosed with migraine.
- This was a cross-sectional study, and causality cannot be concluded from this analysis.

Key Words: major depressive episode, migraine, comorbidity, prevalence

Depression is one of the most common major psychiatric disorders. In 2003, the National Comorbidity Survey Replication reported a lifetime prevalence of CIDI-diagnosed major depression of 16.2% (95%CI, 15.1% to 17.3%) (1). The WHO estimates that, by the year 2020, unipolar major depression will become the second leading cause of disease burden worldwide, second only to ischemic heart disease (2). These data ask for an aggressive approach to identifying factors that may affect the diagnosis of, and treatment strategies for, depression. Among these factors, the complex relation between depression and other medical conditions requires particular attention. In a prospective, community-based study in a Canadian population, Patten described an increased risk of developing depression with almost any long-term conditions and reported that, alternatively, depression may increase the risk of chronic medical conditions (3). Other reports (4–8) support these results. A limited number of studies have addressed the importance of comorbidity between depression and migraine, a chronic condition with a high prevalence rate of 18% for women and 6% for men (9). Although clinicians have recognized an association between depression and migraine, reliable and valid epidemiologic data on the prevalence and incidence of these comorbid disorders are not yet established. With few exceptions (10), most of the population-based studies demonstrated that there is an association between major depression and migraine (7,11–20). They may represent a direct or indirect etiologic effect of one condition on the other, an effect of one condition on the prognosis or mortality associated with the other, or an impact of shared environmental or genetic risk factors.

Canadian epidemiologic data on migraines and major depression have not been available. Also, many of the existing studies have been clinical studies and are not based on probability samples from the general population. In the current study, we investigate the migraine–depression comorbidity patterns in the Canadian general population, using data from the CCHS (21). This is a large-scale epidemiologic study ($n = 131\,535$) supporting estimation of the annual prevalence of major depression in patients with migraine with much more precision than has previously been possible and also supporting stratified analysis.

Abbreviations used in this article

CCHS	Canadian Community Health Survey
CI	confidence interval
CIDI	Composite International Diagnostic Interview
CIDI-SFMD	CIDI Short Form for Major Depression
MDE	Major depressive episode
OR	odds ratio

This analysis provides unprecedented epidemiologic descriptive data on the migraine–major depression comorbidity patterns in a large population sample. This information is essential for planning health services and prioritizing further research in this area.

Methods

The CCHS is a cross-sectional survey conducted by Statistics Canada. The target population for the CCHS survey comprised 22 856 381 Canadian residents within the age-eligibility criteria, that is, approximately 98% of the age-eligible national population. The sample was a probability sample representing the Canadian population, with the exception of military bases, First Nations reservations, and some remote areas in Quebec and Ontario. The target population was also restricted to residents of households. The CCHS interview included inquiries into a broad set of long-term medical conditions. Conditions expected to have a duration greater than 6 months were regarded as long-term conditions. The CCHS data are made available to researchers through regional data centres, one of which is located at the University of Calgary campus, where the current analysis was conducted.

In the CCHS, the CIDI-SFMD was used to evaluate major depression, with the CIDI-SFMD 90% predictive cut-point being used (22). According to this instrument's validation data, the subjects identified as having major depression would have a 90% probability of an MDE in the preceding year. Diagnostic data were collected by self-report. Subjects were asked whether they had been diagnosed with migraine headaches by a health professional in the preceding year. Demographic and other clinical variables were evaluated with standardized questions developed and extensively field-tested by Statistics Canada.

The sampling procedures for the CCHS were complex. These design features have implications for data analysis. The unequal (stratified) sampling creates a requirement to use sampling weights in the analysis. Fortunately, the sample is a probability sample (based on the Labour Force Survey sampling procedures). Sampling weights are provided to researchers by Statistics Canada. The clustering precludes the use of standard statistical methods. In this analysis, we used a bootstrap technique recommended by Statistics Canada to account for the CCHS design effects.

Results

In the target population for the CCHS survey, the weighted sample was 51.0% women and 49.0% men. The age distribution of this sample is shown in Table 1.

The annual prevalence of major depression in the total studied population was 7.4% (95%CI, 7.2% to 7.6%). Consistent with previous studies, the prevalence was higher in female (9.4%;

Table 1 Age and sex distribution of the study population

Age (years)	%
18 to 38 ($n_1 = 8\ 997\ 938$)	
Women	49.6
Men	50.4
39 to 58 ($n_2 = 8\ 814\ 897$)	
Women	50.2
Men	49.8
> 58 ($n_3 = 5\ 043\ 545$)	
Women	54.8
Men	45.2

Table 2 Age-specific prevalence of MDE, chronic conditions other than migraine, and migraine in the CCHS

Conditions and age (years)	Prevalence (%)	95%CI
MDE		
18 to 38	9.0	8.6–9.4
39 to 58	7.8	7.5–8.1
> 58	3.8	3.5–4.1
Chronic conditions		
18 to 38	44.3	43.5–45.1
39 to 58	54.9	54.2–55.6
> 58	80.2	79.5–80.8
Migraine		
18 to 38	10.4	10.0–10.9
39 to 58	10.9	10.5–11.3
> 58	5.1	4.7–5.4

95%CI, 9.1% to 9.7%) than in male subjects (5.3%; 95%CI, 5.1% to 5.6%) and decreased with age (Table 2). The prevalence of any self-reported chronic medical condition (excluding migraine) in the total sample population was 56.3% (95%CI, 55.9% to 56.8%) and, as expected (and unlike migraine prevalence), increased with age (Table 2). The prevalence of reported migraine headaches was 9.4% (95%CI,

9.2% to 9.7%). Migraine prevalence was lower in older subjects.

Our results show a considerable elevation of the prevalence of major depression in subjects reporting migraines, compared with the prevalence of major depression in the general population or in subjects with other chronic medical conditions (17.6%, compared with 7.4% and 7.8%, respectively; Table 3). In the group reporting chronic conditions but not migraines, the prevalence was only slightly elevated relative to the general population, and CIs for the prevalence estimates in these 2 groups overlapped, suggesting that the small difference could be due to sampling variability.

We obtained further clarification of the underlying epidemiology with stratified analysis (Table 4). The population was divided into 3 groups, and adequate within-stratum sample numbers were maintained to support precise estimation. The stratified analysis showed that, as expected, having a chronic condition other than migraine was significantly associated with major depression in subjects aged 18 to 38 years but not in the older age group. The association of migraine headache with an MDE was robust, persisting across all age strata (Table 4).

To evaluate the observed effects further, we developed a logistic regression model. The initial model included a term depicting the possible migraine \times age > 58 years \times sex interaction. The interaction term was not significant at the $P < 0.05$ level (Wald test statistic 3.20, $P = 0.07$). We therefore deleted this term from the final analysis, which is presented in Table 5. The model indicates that, after controlling for the effect of age and sex, those with migraines have a 2.6 times greater prevalence of major depression than those without migraines.

Discussion

This analysis confirms a strong association between migraines and major depression in a general population sample. The results presented here suggest not only that migraines are strongly associated with major depression but also that 1) the migraine–MDE association accounts for a sizable proportion of the chronic condition–MDE association at the population level and 2) the association between migraines and MDE differs from that of other chronic conditions, as the association persists into older age groups.

Previous studies have reported prevalence ratios or ORs for the association between chronic conditions generally and major depression as being in the range of 1.5 (3,7,23–25), but this study shows that the association between MDE and migraine is much stronger. Partly for this reason and partly because migraines are so common in the general population, migraine headaches appear to make a disproportionate contribution at the population level, relative to other chronic

Table 3 Prevalence of MDE in the CCHS

	MDE prevalence (%)	95%CI
General population	7.4	7.2–7.6
Migraine	17.6	16.6–18.6
Other chronic conditions	7.8	7.5–8.0

Table 4 Age-stratified analysis of MDE associations with migraine and other chronic conditions

Conditions	MDE prevalence (%)	95%CI
Age 18 to 38 years		
General population	9.0	8.6–9.4
Migraine	19.6	18.0–21.2
Chronic diseases	10.7	10.1–11.3
Age 39 to 58 years		
General population	7.8	7.5–8.2
Migraine	17.6	16.1–19.2
Chronic diseases	8.6	8.1–9.1
Age > 58 years		
General population	3.8	3.5–4.1
Migraine	10.2	8.2–12.3
Chronic diseases	3.8	3.5–4.2

conditions. Nearly 10% of the population report migraine headaches, and these have a greater than twofold increase in the prevalence of major depression.

In our study, the prevalence of both MDE and migraine decreases with age. In contrast, as expected, the prevalence of chronic conditions increases with increased age. Our results are consistent with previous surveys reporting a decrease of MDE prevalence in older age groups (1). Most recent population-based studies also agree with our results, reporting a decreased prevalence of migraine with increased age across most of the adult lifespan. Possible mechanisms for the lower prevalence of migraine with increasing age have been considered, such as increased mortality in patients with migraine, the favourable effect of preventive treatments, cohort effect, and spontaneous remission (26). Since migraine has a high prevalence in the age groups where major depression is most prevalent, adjustment for age using logistic regression did not weaken the observed association. In other words, age did not

confound the association between major depression and migraine.

From a clinical perspective, migraine and depression resemble each other in some respects, both being episodic disorders that can be highly debilitating in the absence of objective markers (27). This could create stigma associated with both disorders, which might make patients reluctant to seek help, delaying diagnosis and treatment. Depression may potentially be underdiagnosed in migraine sufferers because it may present differently than it does in persons without migraine. Clinicians may fail to inquire about or may minimize depressive symptoms because they may consider them to be normal adaptations to the pain associated with migraine headaches. Failure to recognize comorbid depression can result in suicide. It has been shown that the rates of suicidal ideation and attempts were significantly higher in patients with comorbid depression and migraine with aura than in persons with either disorder alone (28). From this perspective, the clinical and public health implications of our results are threefold. First, clinicians should have a high index of suspicion for depression in persons with migraines and vice versa, irrespective of their age and sex. Second, services for people with migraines should plan for access to psychiatric consultation and expertise. Third, because migraines appear to have a substantial impact on population mental health, there may be a role for public health interventions, such as public education or screening programs targeting the general population. A review study by Katon concluded that there was a 50% increase in medical costs for patients with comorbid major depression and chronic medical conditions, compared with patients with chronic conditions alone (29). Therefore, the mentioned interventions might ultimately have an affect not only on the well-being of the patients but also on the social and economic burden of these comorbid disorders.

Because the analysis presented here is based on cross-sectional epidemiologic data, the associations should not be interpreted as causal. Several potential mechanisms could explain the association found between MDE and migraine. An impact of major depression on migraine risk, an impact of migraines on major depression risk, or an impact of one condition on the prognosis of the other could all account for the observed association. A recent prospective study reported that major depression did not influence the prognosis of migraine (30). In contrast to the Baltimore Epidemiologic Catchment Area study (14), which reported no association between major depression and the incidence of migraine, Breslau and others concluded not only that preexistent migraine increases the risk for first onset of depression but also that the relation is bidirectional, with each disorder increasing the risk of first onset of the other (30). These results suggest a shared-etiology hypothesis rather than a

Table 5 Logistic regression model: MDE and migraine association adjusted for age and sex

	OR	95%CI
Migraine	2.6	2.4–2.8
Men	—	—
Women	1.7	1.7–1.8
Aged 18 to 38 years	2.4	2.2–2.6
Aged 39 to 58 years	2.0	1.8–2.2
Aged 59 years and over	—	—

unidirectional causal one. Although there are no unambiguous conclusions regarding the molecular basis of either migraine or major depression, there is evidence for the involvement of serotonin receptors and transporters, dopamine receptors, and adrenaline in both diseases (31–35). Munro and Munro proposed an interesting hypothesis by which a potential link between chronic pain and depression involves a chronic stress-induced hypothalamo–pituitary–adrenal axis dysfunction mediated by molecular targets, including monoamines (36). Recent studies suggest the efficiency of known antidepressant drugs (that act at the level of some of these neurotransmitters), including amitriptyline (37), bupropion (38), trazodone (39), and venlafaxine XR (40), in the prevention or treatment of migraine. The mainstream treatment of migraine includes triptans, which are serotonin agonists (41). It has also been suggested that triptan treatment of migraine may decrease the depression level, independent of antidepressant treatment (42). Therefore, it is tempting to speculate that, in the end, the 2 conditions may share common pathophysiological substrates.

This study has several limitations. First, the presence of migraine was self-reported and not diagnosed according to the criteria of the Headache Classification Committee of the International Headache Society (43). Some patients suffering from chronic headaches might have then tallied as migraine sufferers. Second, as mentioned already, this is a cross-sectional study, and causality cannot be determined from this analysis. A prospective study would provide more conclusive information regarding the incidence of MDE in people with migraines.

The main strength of this study is that, because of the high participation rate and the sampling procedure, the results can be interpreted as representative of all Canadians and are less susceptible to the bias of clinical samples.

In conclusion, the data reported here provide insights into the importance of awareness, on the part of both health care

clinicians in routine clinical setting and mental health clinicians, regarding the increased association between MDE and migraine in all age groups. Clinicians are challenged to recognize that MDE and migraine may coexist; this should be taken into account when treatment strategies are developed.

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Résumé : Comorbidité de la dépression majeure et de la migraine — une étude de la population canadienne

Objectif : Estimer la prévalence des épisodes de dépression majeure (EDM) chez les patients souffrant de migraine et comparer le degré d’association de celle-ci avec d’autres affections médicales de longue durée.

Méthodes : Cette étude a utilisé un échantillon aléatoire à grande échelle (plus de 130 000) de l’Enquête sur la santé dans les collectivités canadiennes (ESCC), une étude transversale menée par Statistique Canada. L’ESCC dépistait une vaste gamme d’affections médicales. La dépression majeure a été évaluée au moyen de la version abrégée de l’entrevue diagnostique composite internationale pour la dépression majeure, et le diagnostic de migraine était auto-déclaré. La prévalence annuelle de la dépression majeure a été calculée dans la population générale, chez les sujets souffrant de migraine, et chez ceux ayant des affections chroniques autres que la migraine.

Résultats : La prévalence de la dépression majeure chez les sujets déclarant la migraine était plus élevée que dans la population générale ou que chez les sujets ayant d’autres affections chroniques (17,6 %, comparativement à 7,4 % et 7,8 %, respectivement).

Conclusions : Il y a une forte association entre la dépression majeure et la migraine. L’association migraine-EDM peut représenter une large portion de l’association affection chronique-EDM. L’association entre la migraine et l’EDM diffère de celle d’avec d’autres affections chroniques, car l’association persiste chez les groupes d’âge plus avancé.