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Possible high fever in influenza outpatients with migraine – A retrospective cohort study

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ABSTRACT

Background. There is limited information on neurologic complications associated with influenza in adults.
Objectives. To identify headache features and high fever in influenza outpatients with migraine in the Department of Internal Medicine by a neurologist.
Methods. In 2022, a retrospective cohort study was performed to review the medical records during 2016 to 2019. A total of 64 (44 women; 53 unvaccinated; 47 type A) influenza patients were included. All patients were physically examined, and axillary temperatures were measured at around 9 am. The mean body temperature in 34 patients without headache was compared to that in 22 with headache and 8 with headache and an underlying migraine.
Results. Among the 27 unvaccinated influenza type A patients (18 women) under 50 years old, the mean body temperatures were 37.79, 38.10, and 38.86 degrees C for the 12 (6 women) without headache, 10 (8 women) with headache, and 5 (4 women) with headache and a history of migraine, respectively. The mean [SD] ages were 33.58 [7.27], 37.30 [9.58], and 32.40 [7.50] years, respectively. Levene`s Test showed no equal variances between the body temperatures of the 12 without headache and those of 5 with headache and a history of migraine (P=0.007). Welch`s Test showed significant differences in their mean body temperatures (P=0.012).
Conclusion. There is a possibility of high fever in unvaccinated influenza type A outpatients under 50 years old with migraine.

Keywords: adult, headache, high fever, influenza A, migraine

INTRODUCTION

Neurologic complications associated with influenza in adults are rarely diagnosed compared with those in children. The rates of those were low in Europe [1,2] and the USA [3]. During the Covid-19 pandemic from 2019 to 2021, several women identified with encephalitis or encephalopathy were reported in those countries [4-7]. Except for pregnant women, high-risk patients and underlying diseases were not identified.

Migraine is a common disease characterized by the recurrence of headache. The prevalence is highest in women. When migraineurs suffer from influenza, it is unclear how headache features and physical findings are affected. Especially in women of reproductive age, menses are a stressful burden and are associated with menstrual migraine [8], menstruation-related headache [9], and perimenstrual migraine [10]. Those are the most important factors worsening migraine. Also, it was reported that fever might occur with migraines in rare cases [11,12]. Little is known about whether migraines cause fever. In this study, a possible risk of high fever is discussed in influenza patients with migraine.

METHODS

In 2022, a retrospective cohort study was performed to review the medical records during 2016 to 2019. An outpatient clinic was provided half-day a week in the Department of Internal Medicine by a neurologist. From January 2016 to December 2019, 434 new patients were physically examined. Among

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them, 134 patients complained of headaches. Only 6.0% of them reported primary headaches. The majority of them reported secondary headaches that were associated with acute systemic viral infection. The rate of headache was highest in those with laboratory-confirmed influenza (46.9%, 30/64), and it was followed by pneumonia (28.6%, 2/7), upper respiratory tract infections (28.2%, 80/284), cough-variant asthma (23.1%, 3/13), infectious gastroenteritis (17.4%, 8/46), and urinary tract infection (10%, 1/10). Two lactating women with mastitis reported headache. In this study, the headache features in influenza patients (age, sex, influenza type, vaccination, and underlying migraine) were identified. All patients were physically examined, and the axillary temperatures were measured at around 9 am.

RESULTS

A total of 64 (44 women; 53 unvaccinated) patients aged 17 to 68 years (mean age, 40.2 years) suffered from influenza type A (47) or type B (17). Among them, 30 (46.9%) patients (22 women; 25 unvaccinated; 25 type A) reported headache as their primary complaint. The incidence of headache differed between virus types and sexes. In total, 54.2% of type A and 25.0% of type B patients and also 51.2% of women and 38.1% of men reported headache. Influenza type A and women were predominant. The prevalence of migraine in women and men was 16.3% (7/43) and 4.8% (1/21), respectively. Among the 30 influenza patients with headache, 31.8% (7/22) of women and 12.5% (1/8) of men had an underlying history of migraine. The total rate of migraine was 26.7% (8/30). This was similar to the total rate of 25.3% (25/99) of patients with COVID-19 [13].

Among the 27 unvaccinated influenza type A patients (18 women) under 50 years old, the mean body temperatures were 37.79, 38.10, and 38.86 degrees C for the 12 (6 women) without headache, 10 (8 women) with headache, and 5 (4 women) with headache and a history of migraine, respectively. The mean [SD] ages were 33.58 [7.27], 37.30 [9.58], and 32.40 [7.50] years, respectively. Levene`s Test showed no equal variances between the body temperatures of the 12 without headache and those of 5 with headache and a history of migraine (P=0.007). Welch`s Test showed significant differences in their mean body temperatures (P=0.012). The 95% CI was -1.068 degrees C (95% CI: -1.860 to -0.276).

DISCUSSION

Neurologic complications associated with influenza were recognized in children. Pre-existing neurologic conditions were an important background to neurologic complications with pandemic influenza type A (H1N1) 2009 infection [14], and 2015-2020 seasonal influenza [15]. Eighteen children with 2009 H1N1 neurologic complications showed seizures, encephalopathy, and status epilepticus [16]. Also, apparently healthy children without underlying diseases exhibited a risk of influenza-associated encephalitis or encephalopathy [17,18]. On the other hand, there is limited information on neurologic complications in adults. The rate of influenza with encephalitis in Sweden between 1987 to 1998 was 1.5 per 1000 hospitalized influenza patients [1]. The rate of neurologic complications in Austria during the season of 2017 to 2018 was 37 (4.2%) out of 874 hospitalized influenza patients, including 24 (2.7%) with encephalitis [2]. The rates of encephalitis in Sweden and Austria were low. However, neurologic complications were very serious and the pathogenesis remains unclear. During the Covid-19 pandemic from 2019 to 2021, several women with influenza were identified with encephalitis or encephalopathy in the USA [4] and Europe [5-7]. Pregnant women showed an increased risk of complications [19]. Except for pregnant women, the risk in women of reproductive age was unclear.

Among many migraineurs, the prevalence is highest in women. Headache triggers in women were: menstruation, stress, and bright lights [20]. Menstrual migraine that is associated with menstruation affects about 20-25% of women migraineurs in the general population [8]. Menstruation-related headache occurred in 41.9% women with migraine [9]. Furthermore, perimenstrual migraine affects women. A longer duration of perimenstrual migraine resulted in recurrence of migraine and drug overuse [10]. During pregnancy, lactation, and menses, sex hormones affect the expression of migraine [21]. It was also reported that fever might occur with migraines in rare cases. A total of 156 (9%) of 1724 children presented with fever together with migraine attack [11]. A 15-year-old girl presented with a recurrent increase in body temperature associated with migraine headache [12]. The mechanism of this symptom remains unknown. It may be associated with hypothalamic dysfunction. In this study, unvaccinated influenza type A outpatients under 50 years old presented with high fever. There is a possibility that migraine may be responsible for increasing the body temperature.

Influenza encephalitis and encephalopathy of women are rare diseases but serious neurologic complications. At present, clinical features of influenza with migraine are unknown, especially during menstrual and perimenstrual period. Further studies in larger groups including influenza type B and both sexes are required to clarify whether some or all types of migraine may be a risk of high fever in influenza patients with headache and are related to neurologic complications.

CONCLUSIONS

Pre-existing neurologic conditions were an important background to neurologic complications associated with influenza in children. There is limited information on neurologic complications in adults. At present, clinical features of influenza with migraine are unknown. In this study, un vaccinated influenza type A outpatients under 50 years old presented with high fever. There is a possibility that migraine may be responsible for increasing the body temperature, especially in women of reproductive age.

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