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# Time Trends of Epidemiology of Hemorrhagic Stroke among Urban Population in Kazakhstan

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**Abstract**

**AIM:** BACKGROUND: Central Asia has been known among the highest hemorrhagic stroke (HS) and subarachnoid hemorrhage (SAH) burden regions globally. Despite the decline in cardiovascular disease mortality, HS and SAH have been remaining a public health concern in Kazakhstan.

**AIM:** This study aimed to evaluate the trends of HS and SAH among the urban population in Kazakhstan.

**METHODS:** We studied HS and SAH cases aged 18 years and older between 2013 and 2017 hospitalized to stroke centers in Almaty (Kazakhstan). HS and SAH were confirmed by neuroimaging. We calculated age-standardized event, mortality and in-hospital case-fatality rates (per 100,000 populations) with 95% confidence intervals for each individual year and over the 5 years using SAS University Edition and Joinpoint Regression Program.

**RESULTS:** Out of 2759 HS and 413 SAH cases admitted into the stroke centers of Almaty (Kazakhstan), 27.4% cases died in a hospital. The age-standardized HS event rates decreased in both sexes over the 5 years while age-standardized SAH event rates increased for the same period of time. The age-standardized mortality and case-fatality rates decreased in women among HS and SAH cases and men with HS. However, the age-standardized mortality and case-fatality SAH rates increased in men over same period.

**CONCLUSIONS:** Despite the overall decline in HS and slight increase in SAH over the 5 years, the burden remains high. We need to further monitor HS and SAH trends to develop targeted interventions and ensure that the preventive strategies are reducing the burden.

## Introduction

Stroke is of leading causes of death worldwide and a major disabling health problem in developing countries [1]. Central Asia has been struggling with high hemorrhagic stroke (HS) and subarachnoid hemorrhage (SAH) incidence, mortality and disability-adjusted life-years rates [2], [3] that impact the region's economy and population quality of life. Kazakhstan is the most economically developed country and has the second largest population in Central Asia. Furthermore, after the collapse of the Soviet Union, Kazakhstan could only launch the series of health reforms, which has started since the 2000s to address the high burden diseases, including cardiovascular disease (CVD) [4]. Furthermore, every citizen, qandas (an ethnic Kazakh-repatriate moving to Kazakhstan from neighboring countries), foreigner and expat who permanently residing in Kazakhstan can receive free medical care, including preventive, diagnostic and therapeutic medical services, under the Guaranteed Volume of Free Medical Care at the expense of budget funds [5]. As a result, each stroke hospitalization covered by the government allowing all citizens unrestricted access to medical care. Despite the decline in CVD mortality, HS and SAH have been remaining a public health concern in Kazakhstan. To foster the evidence-based practice and data-driven decision making in stroke management and care, politicians and clinicians rely on high-quality health-related data that has not been commonly accessible in the country due to the lack of ongoing population-based studies on this topic and poor analytical competence in epidemiological information processing. To fill this gap in HS and SAH monitoring, we attempt to evaluate HS and SAH cases over time in the urban city of Kazakhstan using complex statistical methods. This study aimed to evaluate the trends of HS and SAH among the urban population in Kazakhstan.

## Methods

### *Ethical issues*

The ethics committee of the Local Ethical Committee of the Higher School of Public School approved this study (IRB-A074/A 15.11.2017).

### *Data source and study population*

Almaty city is a former capital city of Kazakhstan with 1.9 million population [6], [7]. The city has four stroke centers that provide acute stroke care for adults and one stroke center for children. The stroke centers were organized on the basis of multidisciplinary clinical hospitals in Almaty. The distribution of bed volume in stroke centers of Almaty is based on the serving population density and looks as following Almaty City Hospital #7 has 115 stroke-beds, Almaty City Hospital #4 30 beds, Almaty Central City Hospital 20 beds, and City Emergency Hospital has 30 stroke-beds. All possible acute stroke onset cases were evaluated by paramedics if the case is at home or by a neurologist in case of the hospital setting based on the approved clinical protocol for stroke diagnosis in Kazakhstan [8]. The final diagnosis is made after head computed tomography or magnetic resonance imaging confirmation and a neurologist or neurosurgeon verification.

Data on HS and SAH were obtained from the Electronic Hospital-Based Database of Almaty Stroke centers in the period of the year January 01, 2013 - December 31, 2017. The database collects health-related, admitted, and discharge data for all stroke hospitalizations in the city. All stroke cases that occurring in non-Stroke hospitals such as general and surgical wards in Almaty are referred to Almaty Stroke centers for treatment after stabilizing patient's health conditions. Stroke cases occurring out-of-hospitals and stroke cases that refused to be hospitalized do not register in this database. Age and sex distributions for Almaty population were obtained from the Statistics committee of Kazakhstan for the corresponding period [6].

We included patients with first-ever HS and SAH aged 18 years and older between January 01, 2013 and December 31, 2017. HS was coded as I.60.0–69.9, 61.0–61.9 and I62.0–62.9 based on International Classification of Disease-10. Ischemic stroke, transient ischemic attack, hemorrhagic transformations, recurrent HS and SAH cases, HS and SAH cases younger than 18 years and non-Almaty residents who had HS and SAH were excluded from the analysis.

The study was approved by the Local Ethical Committee of the Higher School of Public School (IRB-A074/A 15.11.2017).

### *Statistical analysis*

We calculated crude and age-standardized age- and sex-specific event, mortality and in-hospital case-fatality HS and SAH rates (per 100,000 populations) with 95% confidence intervals (CIs) for each individual year and the period between 2013 and 2017. The WHO world standard population [9] was used to adjust for age structure. A direct standardization method was used to compare over time.

Trends in event rate, mortality and in-hospital case-fatality rates over a specified time interval for men and women were analyzed using Joinpoint regression, calculating annual percent change (APC), under the assumption of a Poisson distribution. We performed analyses in MS Excel, SAS University Edition and Joinpoint Regression Program, Version 4.7.0.0 (Statistical Research and Applications Branch, National Cancer Institute).

## Results

There were 2759 HS and 413 SAH cases admitted into the stroke centers of Almaty (Kazakhstan) from 2013 to 2017. Of these admitted patients, 740 (26.8%) HS and 130 (31.5%) SAH cases died in a hospital. However, there is no significant difference ($p \geq 0.05$). The age of all cases ranged from 18 to 98 years. In 2017, the mean age at the onset of HS was 59.5 (SD 12.5) years in men and 63.9 (SD 13.8) years in women; whereas, the mean age for SAH cases for men was 54.1 (13.1) years and 56.7 (14.2) for women, which was a statistically significant event ($p \leq 0.05$).

Likewise, the mean age of those HS cases, who died was 58 (SD 11.6) years in men, and 67.9 (SD 12.2) years in women ($p \leq 0.05$). Among SAH cases, the mean age of those who died was 50.8 (15.9) years for men and 65.7 (11.8) for women ($p \leq 0.05$). There was a slight increase in total numbers of HS events in both men and women, but the total number of death had decreased from 189 in 2013 to 142 in 2017. On the other hand, we see the increase in total numbers of SAH events and mortality during studied period (Tables 1 and 2).

The age-standardized HS event rates in men decreased from 67.1 (59.3–75) to 60.6 (53.9–67.3) per 100000 population with -2.4% (-10.4–6.4) of APC over the 5 years. The highest decrease in HS event rates was seen in the age groups of 15–34 years with -17.2% of APCs. On the contrary, the sex-specific HS event rates increased in age groups of 75+ years with 6.4% (–9.1–24.3) of APCs. In women, the age-standardized HS event rates decreased from 40.4 (35.5–45.2) to 35.1 (31–39.2) per 100000 population with -4.6%

**Table 1: Demographic characteristics in intracerebral hemorrhage stroke event, mortality and case-fatality rates by age and sex**

| Characteristics | 2013 | 2017 | 2013-2017 | 2013 | | 2017 | | 2013-2017 | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | Men | Women | Men | Women | Men | Women |
| Events | | | | | | | | | |
| Age, years, mean (SD) | 60.1 (14.8) | 61.6 (13.3) | 61.1 (13.7) | 57.3 (13.9) | 63.1 (15.1) | 59.5 (12.5) | 63.9 (13.8) | 58.8 (12.9) | 63.5 (14.1) |
| Age groups | | | | | | | | | |
| 15–34 | 32 (5.7) | 18 (3) | 96 (3.5) | 21 (7.2) | 11 (4.1) | 10 (3.1) | 8 (2.9) | 58 (4.1) | 38 (2.8) |
| 35–54 | 158 (28.3) | 142 (23.7) | 734 (26.6) | 95 (32.8) | 63 (23.5) | 80 (25.2) | 62 (22.1) | 432 (30.4) | 302 (22.6) |
| 55–64 | 156 (28) | 198 (33.1) | 842 (30.5) | 90 (31) | 66 (24.6) | 126 (39.6) | 72 (25.6) | 485 (34.1) | 357 (26.7) |
| 65–74 | 115 (20.6) | 132 (22) | 569 (20.6) | 56 (19.3) | 59 (22) | 62 (19.5) | 70 (24.9) | 271 (19.1) | 298 (22.3) |
| 75+ | 97 (17.4) | 109 (18.2) | 518 (18.8) | 28 (9.7) | 69 (25.8) | 40 (12.6) | 69 (24.6) | 176 (12.4) | 342 (25.6) |
| Total | 558 | 599 | 2759 | 290 | 268 | 318 | 281 | 1422 | 1337 |
| Age–adjusted event rates (95% CL) per 100K | 51. 4 (47.1–55.7) | 45.4 (41.8–49.1) | 45.9 (44.2–47.6) | 67.1 (59.3–75.0) | 40.4 (35.5–45.2) | 60.6 (53.9–67.3) | 35.1 (31.0–39.2) | 59.7 (56.6–62.9) | 36.4 (34.5–38.4) |
| Mortality | | | | | | | | | |
| Age, years, mean (SD) | 60.3 (14.3) | 62.3 (12.8) | 62 (13.8) | 58.3 (13.6) | 62.7 (14.8) | 58 (11.6) | 67.9 (12.2) | 59.1 (12.4) | 65.5 (14.4) |
| Age groups | | | | | | | | | |
| 15–34 | 8 (4.2) | 2 (1.4) | 20 (2.7) | 4 (3.9) | 4 (4.7) | 2 (2.5) | – | 10 (2.5) | 10 (3) |
| 35–54 | 55 (29.1) | 34 (23.9) | 186 (25.1) | 37 (35.9) | 18 (20.9) | 22 (27.9) | 12 (19.1) | 126 (31.2) | 60 (17.9) |
| 55–64 | 52 (27.5) | 42 (29.6) | 213 (28.8) | 29 (28.2) | 23 (26.7) | 33 (41.7) | 9 (14.3) | 135 (33.4) | 78 (23.2) |
| 65–74 | 42 (22.2) | 36 (25.4) | 166 (22.4) | 21 (20.4) | 21 (24.4) | 15 (19) | 21 (33.33) | 82 (20.3) | 84 (25) |
| 75+ | 32 (16.9) | 28 (19.7) | 155 (21) | 12 (11.7) | 20 (23.3) | 7 (8.9) | 21 (33.3) | 51 (12.6) | 104 (31) |
| Total | 189 | 142 | 740 | 103 | 86 | 79 | 63 | 404 | 336 |
| Age–adjusted event rates (95% CL) per 100K | 17.5 (15.0–20.0) | 10.8 (9.1–12.6) | 12.4 (11.5–13.3) | 24.2 (19.4–28.9) | 13.0 (10.2–15.8) | 14.9 (11.6–18.2) | 7.8 (5.8–9.7) | 17.1 (15.4–18.8) | 9.1 (8.1–10.0) |
| Case-Fatality | | | | | | | | | |
| Age-adjusted Case-Fatality % (95% CL) | 30.4 (22.1–38.7) | 18.3 (11.0–25.7) | 23.8 (19.6–28.0) | 29.5 (20.2–39.0) | 33.2 (16.9–49.5) | 23.4 (10.6–36.2) | 11.3 (7.4–15.3) | 23.9 (18.8–28.9) | 23.9 (16.6–31.3) |

CI: Confidence interval, SD: Standard deviation.

(–13.5–5.2) of APCs for the same period. All age groups had a decrease in sex–specific HS event rates (Table 2) (p ≤ 0.05).

The age-standardized SAH event rates in men increased from 7.2 (4.7–9.7) to 7.4 (5.1–9.6) per 100000 population with -1.2% (–7.3–5.4) of APC over the 5 years. The highest decrease in SAH event rates was seen in the age groups of 15–34 years with -19% (–43.7–16.5) of APCs. On the contrary, the sex-specific SAH event rates increased in age groups of 55–64 years with 6.1% (-15.2–32.6) of APCs. In women, the age-standardized SAH event rates increased from 6.1 (4.2–8) to 8.2 (6.2–10.2) per 100000 population with 10.3% (-3.2–25.6) of APCs for the same period. All age groups had a increase in sex - specific SAH event rates (p≤0.05), except for age group of 55–64 years with -0.6% (-31.4–44.2) of APCs for the same period (Table 3).

The age-standardized HS mortality rates in men decreased from 24.2 (19.4–28.9) to 14.9 (11.6–18.2) per 100000 population with -12% of APCs between 2013 and 2017. (p ≤ 0.05), The highest decrease in HS mortality rates in men was in the age group of 15–34 years, followed by 65–74 years. The age-standardized HS mortality rates in women decreased from 13 (102.0–15.8) to 7.8 (5.8–9.7) per 100000 population with -12.8% of APCs between 2013 and 2017. The age groups younger than 65 years had

**Table 2: Trends intracerebral hemorrhage stroke event, mortality and case-fatality rates by age and sex**

| Age group | Event rate/100000 | | | Morality rate/100000 | | | Case-Fatality % | | |
|---|---|---|---|---|---|---|---|---|---|
| | 2013 | 2017 | 2013–2017 AAPC (95% CI) | 2013 | 2017 | 2013–2017 AAPC (95% CI) | 2013 | 2017 | 2013–2017 AAPC (95% CI) |
| Men | | | | | | | | | |
| 15–34 | 8,0 (4.6–11.4) | 3,4 (1.3–5.6) | –17.2 (–44.7–23.9) | 1.5 (0.0–3.0) | 0.7 (–0.3–1.7) | –17.9 (–50.1–35.1) | 19,0 (2.3–35.8) | 20.0 (–4.8–44.8) | –0.6 (–17.2–19.3) |
| 35–54 | 54.8 (43.8–65.8) | 39.3 (30.7–47.9) | –7.6 (–15.4–1.0) | 21.3 (14.5–28.2) | 10.8 (6.3–15.3) | –14.8 (–29.7–3.1) | 38,9 (29.2–48.8) | 27,5 (17.7–37.3) | –8.2 (–23.4–10.0) |
| 55–64 | 180.2 (143.0–217.4) | 195.7 (161.5–229,8) | 0.6 (–13.4–16.7) | 58.1 (36.9–79.2) | 51.2 (33.8–68.7) | –5.1 (–22.1–15.6) | 32.2 (22.6–41.9) | 26.2 (18.5–33.9) | –5.5 (–16.1–6.3) |
| 65–74 | 236.0 (31.5–174.2) | 210.6 (26.7–158.2) | –3.4 (–13.5–7.9) | 88.5 (50.7–126.3) | 50.9 (25.2–76.7) | –16.2 (–32.2–3.5) | 37.5 (24.8–50.2) | 24.2 (13.5–34.9) | –12.8 (–23.8—0.2) |
| 75+ | 201.3 (126.8–275.9) | 219.9 (151.8–288.0) | 6.4 (–9.1–24.5) | 86.3 (37.5–135.1) | 38.5 (10.0–67.0) | –12.3 (–36.9–21.9) | 42.9 (24.5–61.2) | 17.5 (5.7–29.3) | –17.2 (–35.3–6.0) |
| All ages* | 67.1 (59.3–75.0) | 60.6 (53.9–67.3) | –2.4(–10.4–6.4) | 24.2 (19.4–28.9) | 14.9 (11.6–18.2) | –12.0* (–21.5—1.3) | 29.5 (20.2–39.0) | 23.4 (10.6–36.2) | –7.5 (–16.9–3.1) |
| Women | | | | | | | | | |
| 15–34 | 3.6 (1.5–5.7) | 2.3 (0.7–4.0) | –8.1 (–32.0–24.3) | 1.3 (0.0–2.6) | 0.3 (–0.3–0.9) | –28.5 (–68.3–61.3.) | 36.4 (7.9–64.8) | 12.5 (–10.4–35.4) | –3.8 (–65.2–165.8) |
| 35–54 | 30.0 (22.6–37.3) | 25.3 (19.0–31.6) | –8.8 (–27.8–15.2) | 8.6 (4.6–12.5) | 4.9 (2.1–7.7) | –17.0 (–43.1–20.9) | 28.6 (17.4–39.7) | 19.5 (9.5–29.2) | –10.1 (–30.2–15.8) |
| 55–64 | 0.09 (0.1–0.1) | 0.08 (0.1–0.1) | –1.3 (0.1–0.1) | 0.03 (0.0–0.0) | 0.01 (0.0–0.0) | –17.9 (–42.5–17.3) | 34.8 (23.3–46.4) | 12.5 (4.9–20.1) | –17.5 (–37.7–9.4) |
| 65–74 | 141.1 (105.1–177.1) | 137.0 (104.9–169.1) | –1.8 (–14.4–12.7) | 50.2 (28.7–71.7) | 41.1 (23.5–58.7) | –6.9 (–28.7–21.5) | 35.6 (23.4–47.8) | 30.0 (19.3–40.7) | –5.2 (–23.3–17.1) |
| 75+ | 214.4 (163.8–265.0) | 169.9 (129.8–210.0) | –6.6 (–18.0–6.3) | 62.1 (34.9–89.4) | 51.7 (29.6–73.8) | –6.0 (–19.6–9.8) | 29.0 (18.3–39.7) | 30.4 (19.6–41.3) | 0.7 (–3.0–4.5) |
| All ages* | 40.4 (35.5–45.2) | 35.1 (31.0–39.2) | –4.6 (–13.5–5.2) | 13.0 (10.2–15.8) | 7.8 (5.8–9.7) | –12.8* (–22.9—1.5) | 33.2 (16.9–49.5) | 11.3 (7.4–15.3) | –24.5* (–35.4—11.7) |

CI: Confidence interval, APC: Annual percent change, *2013-2016 and 2016 for women Age specific mortality rate since no mortality for 2017.

the highest reduction in HS mortality rates in women (p ≤ 0.05) (Table 2).

The age-standardized SAH mortality rates in men increased from 1.9 (0.6–3.1) to 2.5 (1.2–3.9) per 100000 population with 1.7% of APCs between 2013 and 2017 (p ≤ 0.05). The increase in SAH mortality rates among men was seen in the age group older 65 years. The age-standardized SAH mortality rates in women decreased from 2.3 (1.1–3.4) to 1.8 (0.8–2.7) per 100000 population with -4.1% of APCs between 2013 and 2017. The age group 55–64 years had the highest reduction in SAH mortality rates in women (Table 4) (p ≤ 0.05).

The in-hospital case-fatality HS rate in men decreased from 29.5% to 23.4% with -7.5% of APCover 5 years (p ≤ 0.05). Age group 65 years and older had the most contribution to this decrease in men. In women, in-hospital case-fatality rates also decreased from 33.2% to 11.3% with -24.5% of APC (p≤0.05). Age groups younger than 75 years had been contributed to this decline. However, the age group 75+ years showed an increase in in-hospital case-fatality rate (Table 1).

The in-hospital case-fatality SAH rate in men increased from 25.8% to 50.3% with 24.2% of APC over 5 years. In terms of absolute numbers, SAH mortality increased from 9 to 14 cases among men. In women, in-hospital case-fatality rates decreased from 18.6% to 11.1% with -10.5% of APC. The SAH mortality decreased from 15 to 14 cases among women (Table 3).

## Discussion

This study demonstrates that the trend of HS declined while SAH increased among the urban population in Kazakhstan over 5 years, but the burden of HS and SAH is remaining high. The age-standardized HS event, mortality and in-hospital case-fatality rates have decreased in both sexes across most age groups. Although age-specific HS event rate has shown an increase only among the elderly 75+ years in men over 5 years, we would cautiously interpret these findings due to the modest number of HS cases in these groups. Despite the increase of HS events in most age groups, we have seen the reduction in the case-fatality rates among majority of groups both in men and women leading to the overall decline in HS mortality. Conversely, the age-standardized SAH event, mortality and in-hospital case-fatality rates have slightly increased in men across most age groups. In women, the age-standardized SAH event rate has increased but mortality and in-hospital case-fatality rates have slightly decreased across most age groups over 5 years. Overall, we would cautiously interpret the findings on SAH trends due to the modest sample size. However, we recognize that SAH events increased in both sexes over 5 year period and so did the population of Almaty [6].

Sex differences in mortality showed that men were at a greater risk to experience HS events and die than women; whereas, women were at greater risk to have SAH events and die than men. To our knowledge, this is the first study evaluating trends of HS and SAH in age- and sex-specific events, mortality and in-hospital case-fatality rates among the urban population in Kazakhstan.

Our study supports evidence from the recent Global Burden of Disease (GBD) 2016 stroke study where GBD demonstrates the decline in stroke trend in Central Asian countries over three decades despite the population growth and increase in the aging population [10]. Although Shah *et al*. [11] reported a recent increase in stroke mortality among most Central Asian countries using the European Standard Population for comparison; Kazakhstan has still shown

**Table 3: Demographic characteristics in subarachnoid hemorrhage stroke event, mortality and case-fatality rates by age and sex**

| Characteristics | 2013 | 2017 | 2013-2017 | 2013 | | 2017 | | 2013-2017 | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | Men | Women | Men | Women | Men | Women |
| Events | | | | | | | | | |
| Age, years, mean (SD) | 54.9 (14.2) | 55.7 (14) | 55.9 (14.5) | 50.8 (14.5) | 58.3 (13.1) | 54.1 (13.8) | 56.7 (14.2) | 54.8 (14.3) | 56.7 (14.7) |
| Age groups | | | | | | | | | |
| 15–34 | 6 (8.2) | 8 (7.7) | 33 (8) | 5 (15.2) | 1 (2.5) | 3 (7.3) | 5 (7.9) | 16 (8.8) | 17 (7.3) |
| 35–54 | 26 (35.6) | 39 (37.5) | 156 (37.8) | 13 (39.4) | 13 (32.5) | 16 (39) | 23 (36.5) | 70 (38.7) | 86 (37.1) |
| 55–64 | 23 (31.5) | 30 (28.9) | 110 (26.6) | 8 (24.2) | 15 (37.5) | 15 (36.6) | 15 (23.8) | 52 (28.7) | 58 (25) |
| 65–74 | 11 (15.1) | 17 (16.5) | 65 (15.7) | 6 (18.2) | 5 (12.5) | 4 (9.8) | 13 (20.6) | 27 (14.9) | 38 (16.4) |
| 75+ | 7 (9.6) | 10 (9.6) | 49 (11.9) | 1 (3) | 6 (15) | 3 (7.3) | 7 (11.1) | 16 (8.8) | 33 (14.2) |
| Total | 73 | 104 | 413 | 33 | 40 | 41 | 63 | 181 | 232 |
| Age-adjusted event rates (95% CL) per 100K | 6.6 (5.1–8.2) | 7.7 (6.4–9.4) | 6.8 (6.1–7.5) | 7.2 (4.7–9.7) | 6.1 (4.2–8.0) | 7.4 (5.1–9.6) | 8.2 (6.2–10.2) | 7.4 (5.1–9.6) | 6.5 (5.6–7.3) |
| Mortality | | | | | | | | | |
| Age, years, mean (SD) | 57 (13.8) | 58.6 (15.7) | 57.4 (13.3) | 47.9 (11.9) | 62.5 (12.1) | 50.8 (15.9) | 65.7 (11.8) | 53.2 (13.2) | 61.1 (12.4) |
| Age groups | | | | | | | | | |
| 15–34 | 1 (4.2) | 2 (7.1) | 6 (4.6) | 1 (11.1) | – | 2 (14.3) | – | 5 (8.2) | 1 (1.5) |
| 35–54 | 8 (33.3) | 10 (35.7) | 51 (39.2) | 5 (55.6) | 3 (20) | 7 (50) | 3 (21.4) | 29 (47.5) | 22 (31.9) |
| 55–64 | 8 (33.3) | 5 (17.9) | 33 (25.4) | 2 (22.2) | 6 (40) | 2 (14.3) | 3 (21.4) | 15 (24.6) | 18 (26.1) |
| 65–74 | 4 (16.7) | 7 (25) | 24 (18.5) | 1 (11.1) | 3 (20) | 2 (14.3) | 5 (35.7) | 9 (14.8) | 15 (21.7) |
| 75+ | 3 (12.5) | 4 (14.3) | 16 (12.3) | – | 3 (20) | 1 (7.1) | 3 (21.4) | 3 (4.9) | 13 (18.8) |
| Total | 24 | 28 | 130 | 9 | 15 | 14 | 14 | 61 | 69 |
| Age-adjusted event rates (95% CL) per 100K | 2.2 (1.3–3.1) | 2.1 (1.3–3.0) | 2.2 (1.8–2.5) | 1.9 (0.6–3.1) | 2.3 (1.1–3.4) | 2.5 (1.2–3.9) | 1.8 (0.8–2.7) | 2.4 (1.8–3.0) | 1.9 (1.5–2.4) |
| Case-Fatality | | | | | | | | | |
| Age-adjusted | 26.0 | 26.0 | 26.3 | 25.8 | 18.6 | 50.3 | 11.1 | 34.1 | 19.1 |
| Case-Fatality % (95% CL) | (9.4–42.5) | (9.7–42.4) | (19.1–33.6) | (4.7–46.9) | (7.6–29.6) | (8.1–92.6) | (4.7–17.6) | (20.9–47.3) | (12.5–25.8) |

CI: Confidence interval, SD: Standard deviation.

a decline in HS mortality rate over three decades. The decline in HS and SAH mortality among the urban population in Kazakhstan could be partially explained by the improvement of population socioeconomic status as well as healthcare services and quality of care through the implementation of State programs on healthcare reforms, which have been prioritized on CVD management and care, since 2005 [4]. Specifically, most attention has focused on the CVD control and prevention such as better control of risk factors, access to essential medicines to treat hypertension, diabetes, and dyslipidemia as well as opening of 36 stroke centers across the country and implementation of clinical guidelines for CVD treatment [12]. For instance, Almaty has four stroke centers that provide care for acute patients. As a result, we have seen a decline in stroke rates, especially among the urban population. This trend is consistent with that of Avan *et al*. [13] who speculates that improved infrastructure, health literacy, and healthcare access have contributed to stroke mortality decline globally, especially in less wealthy regions. In addition to the healthcare service advances, we think that this decline might be due to the reduction of excessive alcohol consumption over the decade in the country. Davletov *et al*. speculates that early CVD deaths in Kazakhstan could be related to the higher prevalent alcohol drinking behavior, which was evident while comparing low- and high alcohol-consuming regions in Kazakhstan [14]. Likewise, a Nationwide survey on the prevalence of behavioral risk factors among adolescents and adult population in Kazakhstan has shown a gradual decrease in average alcohol consumption from 55% in 1998 to 41.9 % in 2007, to 24.2% in 2015 [15], [16].

Despite the decline in HS and increase in SAH event, mortality and in-hospital case-fatality rates, Kazakhstan still has a high burden of stroke-related mortality. A possible explanation for this might be the high prevalence of risk factors such as hypertension, diabetes, smoking, obesity, physical inactivity, and excessive alcohol consumption that have contributed to the stroke rate. For example, the INTERSTROKE study shows that approximately 90% of the population-attributable risk was due to the most above mentioned risk factors [17]. To support that, recently published papers demonstrated that Kazakhstan had a high prevalence of CVD risk factors, which were increase or stable high or slightly decrease overtime [14], [18], [19], [20]. Interestingly, reduction in alcohol consumption was the only risk factor that has significantly decreased over the decade [15], [16]. Taking into account that Almaty is the largest economically developed city in Kazakhstan, its population has been going through the rapid globalization impact, being exposed to Westernized food habits and poor physical activity [18]. Despite that fact, Almaty have a good access to healthcare services, including quality of care than other cities in Kazakhstan [20], [21], [22]; therefore, this might compensate in some cases to the lower event, mortality and in-hospital case-fatality HS and SAH rates among these populations.

Sex-specific mortality HS ans SAH rates were significantly different between men and women among urban population over 5 years. This was consistent with the previous studies [11]. Differences between mortality according to sex could be explained by the cultural perception and behavioral difference between men and women in Kazakhstan, particularly men have a higher prevalence of the risk factors than women as well as women are more likely to seek a proper medical care than men. These thoughts seem to be consistent with other research, which show significant differences in risk factors prevalence between men and women in Kazakhstan [13], [14], [19], [20], [21].

Although this study includes well-defined HS and SAH cases of the Almaty population over 5 years from the hospital-based database, it also has a few limitations. First, since we could not access to mortality database of Almaty, we may have missed some HS and SAH cases that died before reaching the hospital. Consequently, our results on event rates and mortality might be slightly underestimated. Next, we did not have information on HS and SAH severity and comorbidities of the patients to assess the reduction in in-hospital case-fatality rates overtime.

We did not have access to those HS and SAH cases occurring in the Almaty residents that were hospitalized out of the city. We also do not have information on post-stroke survivors to evaluate

**Table 4: Trends in subarachnoid hemorrhage event. mortality and case-fatality rates by age and sex**

| Age group | Event rate/100000 | | | Morality rate/100000 | | | Case-Fatality % | | |
|---|---|---|---|---|---|---|---|---|---|
| | 2013 | 2017 | 2013-2017 AAPC (95% CI) | 2013 | 2017 | 2013-2017 AAPC (95% CI) | 2013 | 2017 | 2013-2017 AAPC (95% CI) |
| Men | | | | | | | | | |
| 15–34 | 1.9 (0.2–3.6) | 1.0 (–0.1–2.2) | –19.0 (–43.7–16.5) | – | – | – | – | – | – |
| 35–54 | 7.5 (3.4–11.6) | 7.9 (4.0–11.7) | –3.1 (–22.0–20.5) | 2.9 (0.4–5.4) | 3.4 (0.9–6.0) | –3.1 (–30.9–35.7) | 38.5 (12.0–64.9) | 43.7 (19.4–68.1) | 0.0 (–11.6–13.1) |
| 55–64 | 16.0 (4.9–27.1) | 23.3 (11.5–35.1) | 6.1 (–15.2–32.6) | 4.0 (–1.5–9.5) | 3.1 (–1.2–7.4) | –11.1(–41.9–36.1) | 25.0 (–5.0–55.0) | 13.3 (–3.9–30.5) | –11.4 (–50.9–60.0) |
| 65–74 | 25.3 (5.1–45.5) | 13.6 (0.3–26.9) | –5.7 (–35.7–38.4) | 4.2 (–4.0–12.5) | 6.8 (–2.6–16.2) | 11.2 (–30.4–77.9) | 16.7 (–13.1–46.5) | 50.0 (1.0–99.0) | 2.0 (–46.0–92.9) |
| 75+ | 43.1 (8.6–77.7) | 38.5 (10.0–67.0) | 10.8 (–37.0–94.8) | 7.2 (–6.9–21.3) | 11 (–4.2–26.2) | 5.2 (–43.9–97.5) | 50.0 (–19.3–119.3) | 50.0 (1.0–99.0) | 1.3 (–34.0–55.6) |
| All ages* | 7.2 (4.7–9.7) | 7.4 (5.1–9.6) | –1.2(–7.3–5.4) | 1.9 (0.6–3.1) | 2.5 (1.2–3.9) | 1.7 (–15.4–22.3) | 25.8 (4.7–46.9) | 50.3 (8.1–92.6) | 24.2* (2.4–50.7) |
| Women | | | | | | | | | |
| 15–34 | 0.3 (–0.3–1.0) | 1.5 (0.2–2.7) | 27.2 (–37.9–160.7) | – | – | – | – | – | – |
| 35–54 | 6.2 (2.8–9.5) | 9.4 (5.6–13.2) | 10.5 (–3.7–26.8) | 1.4 (–0.2–3.0) | 1.2 (–0.2–2.6) | 5.9 (–32.1–65.2) | 23.1 (0.2–46) | 13.0 (–0.7–26.8) | 0.3 (–41.7–72.5) |
| 55–64 | 20.0 (9.9–30.2) | 16.5 (8.2–24.8) | –0.6 (–31.4–44.2) | 8.0 (1.6–14.4) | 3.3 (–0.4–7.0) | –21.6 (–41.3–4.8) | 40.0 (15.2–64.8) | 20.0 (–0.2–40.2) | –16.6 (–46.0–28.6) |
| 65–74 | 12.0 (1.5 –22.4) | 25.4 (11.6–39.3) | 16.6 (–10.2–51.3) | 7.2 (–0.9–15.3) | 9.8 (1.2–18.4) | 9.1 (–22.4–53.3) | 60.0 (17.1–102.9) | 38.5 (12.0–64.9) | –9.0 (–27.0–13.6) |
| 75+ | 18.6 (3.7–33.6) | 17.2 (4.5–30.0) | 11.9 (–36.7–97.7) | 9.3 (–1.2–19.9) | 7.4 (–1.0–15.8) | –2.8 (–22.7–22.3) | 50.0 (10.0–90.0) | 42.9 (6.2–79.5) | –8.6 (–38.0–34.6) |
| All ages* | 6.1 (4.2–8.0) | 8.2 (6.2–10.2) | 10.3 (–3.2–25.6) | 2.3 (1.1–3.4) | 1.8 (0.8–2.7) | –4.1 (–15.1–8.3) | 18.6 (7.6–29.6) | 11.1 (4.7–17.6) | –10.5 (–33.7–20.7) |

CI: Confidence interval, APC: Annual percent change, *2013-2016 and 2016 for women Age specific mortality rate since no mortality for 2017.

follow-up trends in short- and long-term outcomes after the type of received interventions. We were limited with a modest sample size on SAH cases to draw an adequate conclusion. Finally, these findings can be extrapolated only to urban settings in Kazakhstan that have stroke centers because acute stroke care in rural settings are organized differently.

Our study may help us to understand the HS and SAH trends among the urban population in Kazakhstan to better allocate and plan resources in acute stroke care as well as assess interventions and monitor stroke rates overtime. Furthermore, preventive efforts have to be focused on the wide implementation and promotion of the proven interventions such as sodium-lowering, hypertension and diabetes management programs to reduce CVD risk factors, especially among high-risk groups. Likewise, preventive strategies have to focus on behavioral interventions such as reducing alcohol drinking and smoking cessation, especially continue to increase alcohol taxation and pricing policies in the country.

## Conclusion

Despite the overall decline in HS trends over the 5 years, and increase in SAH events, the burden remains high. Thus, we need to further continuously monitor the event rates, mortality, and case-fatality trends to ensure that the targeted interventions and preventive strategies are reducing hemorrhagic stroke burden. Public health professionals have to collaborate with clinicians, policymakers as well as with the community in addressing HS and SAH burden. Since we did not look at the other subtypes of stroke, short- and long-term post-stroke outcomes and trends in the rural population; therefore, future studies have to fill out these gaps.

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