VOLUME 13 • 2020

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KANSAS JOURNAL of MEDICINE

Guideline Adherence in Dyspepsia Investigation and Treatment

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Received July 1, 2020; Accepted for publication Aug. 20, 2020; Published online Dec. 11, 2020
https://doi.org/10.17161/kjm.vol13.13838

ABSTRACT

Introduction. The impact of dyspepsia guidelines on clinical practice may be poor. Provider adherence with dyspepsia guidelines was examined to determine their impact on clinical practice.

Methods. Provider adherence with the 2005 American College of Gastroenterology Guidelines for the Management of Dyspepsia and the 2017 American College of Gastroenterology and Canadian Association of Gastroenterology joint Dyspepsia Management Guidelines was assessed on a national level using data from the National Ambulatory Medical Care Survey (NAMCS). Patient visit data, including reason for visit of dyspepsia, diagnosis of dyspepsia, or diagnosis of *H. pylori* infection from NAMCS years 2012 through 2015, were used. Provider adherence with dyspepsia management guidelines was determined based upon provision of at least one recommended test or treatment for dyspepsia.

Results. Providers appeared to adhere to the 2005 ACG guidelines for 49.7% of patient visits. Providers appeared to adhere to the 2017 ACG/CAG guidelines for 51.0% of patient visits.

Conclusion. Provider adherence with the 2005 ACG and the 2017 ACG/CAG Dyspepsia Management Guidelines was determined to be low in this study, highlighting the need to increase evidence-based medical treatment and efficient resource use for dyspepsia.

Kans J Med 2020;13:306-310

INTRODUCTION

Dyspepsia has been described as epigastric pain persisting for one month or more, which may be associated with a range of other clinical gastrointestinal symptoms, including heartburn or epigastric fullness.[1] The prevalence of uninvestigated dyspepsia in North America is approximately 22%, with a suggested incidence of 1.3% annually and peak incidence in the seventh decade of life.[2,3]

Dyspepsia patients can be categorized as (1) uninvestigated if they have not undergone investigation in an attempt to discover underlying disease, (2) investigated, which exposed a cause for their symptoms, or (3) investigated, but no cause was discovered, termed functional dyspepsia, a diagnosis of exclusion.[4] Investigation by endoscopy revealed clinically significant findings in 10.2% of patients, with one study suggesting nonerosive gastritis and another suggesting reflux esophagitis most commonly, were identified.[5,6] Other underlying causes of dyspepsia included infection of *Helicobacter pylori* (*H. pylori*), gastric or duodenal ulcers, and gastrointestinal malignancy, although functional dyspepsia is the most common cause.[4,7]

Different tests and procedures may be done to investigate dyspepsia symptoms, some of which are not recommended routinely and may increase healthcare costs for dyspepsia management. Among patients diagnosed with functional dyspepsia, the cost of testing received was estimated to be $582 per patient.[8] These patients underwent blood work (75%), abdominal ultrasound (59%), abdominal x-ray (47%), or abdominal and/or pelvis computed tomography (CT; 40%).[8] None of these tests are recommended routinely for evaluation of dyspepsia by either the 2005 American College of Gastroenterology clinical guidelines or the 2017 American College of Gastroenterology and Canadian Association of Gastroenterology joint guidelines.[1,9]

The impact of dyspepsia guidelines on clinical practice may be poor. A vignette survey suggested 57% of primary care providers and 74% of gastroenterologists adhered to the 2005 ACG guidelines and other consensus recommendations for dyspepsia investigation and management.[10]

Endoscopy may be overutilized to investigate dyspepsia. One study suggested 37.8% of esophagogastroduodenoscopies (EGD) done for gastrointestinal indications, including dyspepsia, were not indicated by guidelines.[11] A study of dyspepsia patients younger than 55 years without alarm symptoms suggested 58% (rather than 100%) had received both *H. pylori* testing and proton pump inhibitors (PPI) therapy, as the guidelines recommended, before receiving an EGD.[12] However, endoscopy may be underutilized in older age groups, as one study reported 81% of dyspepsia patients 50 years or older had not received endoscopy, despite guideline recommendations.[13] Another study reported similar results; only 27% of dyspepsia patients older than 55 years had received an EGD, rather than 100% if the 2005 guidelines had been followed.[3]

The current study examined dyspepsia investigation and treatment practices for 2012 - 2015. Provider practices were determined to be adherent or nonadherent with the 2005 ACG Guidelines for the Management of Dyspepsia. Adherence with the 2017 ACG and CAG guidelines also was assessed to determine if clinical practices in the years preceding the release of these guidelines had shifted toward utilizing therapies included in the 2017 guidelines, as new knowledge on effective management was identified, but before updated guidelines were released.

METHODS

Participants. Data were analyzed from the National Ambulatory Medical Care Survey (NAMCS) for 2012 - 2015.[14] Data collected about community health centers were not included. Patient data meeting the following criteria were included: reason(s) for visit including dyspepsia, diagnosis of dyspepsia, or diagnosis of *Helicobacter pylori* infection. Data were excluded if patients were younger than 18 years, or if the patient had a diagnosis of gastroesophageal reflux disease (GERD).

Instrument. Non-federally employed, practicing physicians (excluding pathologists, radiologists, and anesthesiologists) working

in ambulatory care settings in the U.S. were eligible to participate in NAMCS. Physician interviews were used to collect physician and healthcare practice data (e.g., specialty, location). Physicians were surveyed for a sample of patient visits during a random one-week period annually. Data recorded about patient visits included demographic information, patient comorbidities, reason(s) for visit, diagnoses related to the visit, services ordered or provided, medications (including prescription and over-the-counter drugs) ordered or provided, and if these medications were new or continued. Drug information, including drug therapeutic classes, for medications ordered or provided during the patient visit, was coded by NAMCS using Lexicon Plus®, a Cerner Multum™, Inc. database.[15]

The variables used from the NAMCS database files for the current study included patient age, body mass index (BMI), sex, unimputed race, unimputed ethnicity, tobacco use, depression comorbidity, reason for visit, diagnoses related to visit, services ordered or provided, and therapeutic class codes for medications ordered or provided. Up to five reasons for visit and five diagnoses could be listed per patient record. For services not specifically listed as a checkbox item on the patient record interview form, up to nine write-in procedure codes could be documented. Up to 10 medications could be listed for years 2012 and 2013, and up to 30 medications could be listed for years 2014 and 2015. For each medication, up to four categories, with three levels per category, could be used to list the drug's therapeutic class codes from the Lexicon Plus® database.[15]

Data about the physician, including specialty and region of practice within the U.S., were used. Physician specialty was stratified into 14 groups, including general/family practice, internal medicine, and general surgery. Physician specialty was stratified separately into three groups: primary care, surgical care, or medical care specialties. Regions of practice included the northeast, midwest, south, and west regions of the U.S.

Procedures. This study was considered "not human subjects" by the University of Kansas School of Medicine-Wichita's Human Subjects Committee. To assess the frequency of medications ordered or prescribed, drug therapeutic class codes were used. Drug therapeutic classes of interest included antacids, PPIs, H2 antagonists, *H. pylori* eradication agents, gastrointestinal stimulants, and tricyclic antidepressants (TCA).

The frequency of a diagnosis of *H. pylori* infection (ICD-9-CM code 041.86) along with one or more write-in procedure codes encompassing noninvasive *H. pylori* testing recommended by the 2007 ACG *H. pylori* management guidelines was used to determine the frequency *H. pylori* tests were ordered or provided[16] (Table 1).

Table 1. Patient characteristics.

89.39	Other nonoperative measurements and examinations (including 14 C-Urea breath test).
90.59	Other microscopic examination of blood.
90.99	Other microscopic examination of specimen from lower gastrointestinal tract and of stool.
91.39	Other microscopic examination of specimen from bladder, urethra, prostate, seminal vesicle, perivesical tissue, and of urine and semen.

To assess the frequency of EGD or other upper gastrointestinal endoscopy ordered or provided during a patient visit, data from the checkbox item "upper gastrointestinal endoscopy/EGD" for years 2014 and 2015 were combined with write-in upper endoscopy ICD-9-CM procedure codes for years 2012 through 2015 (Table 2). The combined frequency of the EGD checkbox item and the upper endoscopy procedure codes was used to assess the number of upper endoscopies ordered or performed.

Table 2. Write-in upper endoscopy ICD-9-CM procedure codes.

42.23	Other esophagoscopy (excludes that with biopsy).
42.24	Closed [endoscopic] biopsy of esophagus.
44.13	Other gastroscopy (excludes that with biopsy).
44.14	Closed [endoscopic] biopsy of stomach.
45.13	Other endoscopy of small intestine (includes EGD).
45.16	EGD with closed biopsy.

To assess provider adherence with the 2005 ACG guidelines, the provision of at least one component of the 2005 guidelines constituted adherence. Specifically, the provision of any upper endoscopy/EGD, acid suppression medication (PPIs), *H. pylori* eradication agents, or noninvasive *H. pylori* testing was assessed per patient to determine provider guideline adherence (Figure 1). To assess provider adherence with the 2017 ACG/CAG guidelines, the provision of at least one component of the 2017 guidelines constituted adherence. All components of the 2005 guidelines were included in the 2017 assessment, with the addition of tricyclic antidepressant medications, GI stimulant/prokinetic medications, or psychotherapy (Figure 1). H2 antagonists were included as acceptable acid suppression therapy for adherence with the 2005 and 2017 guidelines in two additional assessments of provider adherence.

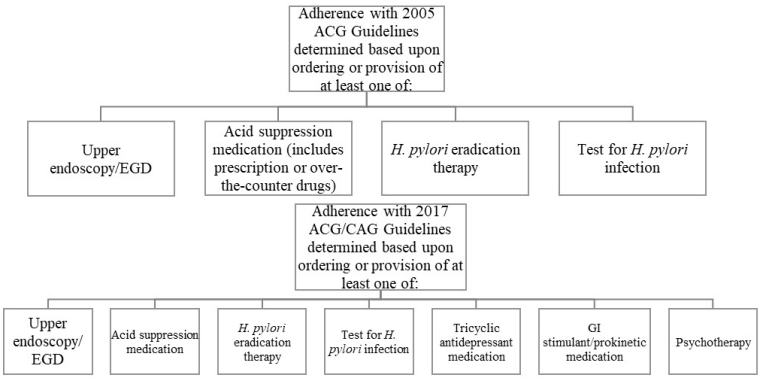

Figure 1. Criteria for guideline adherence.

Analysis. Data were analyzed using SAS version 9.4 (2019, SAS Int. Inc., Carry, NC). Frequencies, proportion, means, and standard deviations were calculated. Pearson chi-square and likelihood chi-square were used to test the associations between categorical variables. Cochran-Mantel-Haenszel statistics were conducted to determine the relationships between two stratified categorical variables after controlling for at least one variable. These stratified analyses

provided a way to adjust for the possible confounding effects without being forced to estimate parameters for them. All statistical tests at $p \leq 0.05$ were considered significant.

RESULTS

Of the 260,118 patient encounters from 2012 through 2015, 680 records met inclusion/exclusion criteria. Of the 680 records, heartburn and indigestion (dyspepsia; ICD-9-CM code 1535.0) was documented as the reason for 58.5% of patient visits (n = 398). The diagnosis of dyspepsia or other specified disorders (ICD-9-CM code 536.8) was listed for 38.2% of patients (n = 260), and the diagnosis of *H. pylori* infection (ICD-9-CM code 041.86) was listed for 13.1% of patients (n = 89).

Physician participants worked throughout the U.S., with 34.4% practicing primarily in southern states (n = 234), 23.1% in western states (n = 157), 23.1% in the midwest (n = 157), and 19.4% in the northeast (n = 132). Broadly grouped, 49.0% of physicians (n = 333) were in medical care specialties, 42.2% of physicians (n = 287) were in primary care specialties, and 8.8% of physicians (n = 60) were in surgical care specialties. Of the 14 specialty groupings, many physicians (41.0%, n = 194) were categorized into the "other" specialties group, which included gastroenterology. Physicians in the "general or family practice" group made up 20.9% of participants (n = 99), and those in internal medicine made up another 20.9% of participants (n = 99).

As reported by their physicians, most patients (82.3%, n = 415) were White, and 9.9% of patients (n = 50) were Black or African American. Almost 20% of patients (18.2%, n = 88) were reported to be Hispanic or Latino (Table 3).

Table 3. Patient demographics.

	Frequency	Percent
Sex		
Female	411	60.4%
Male	269	39.6%
Ethnicity		
Not Hispanic/Latino	396	81.8%
Hispanic/Latino	88	18.2%
Missing	196	
Race		
White/Caucasian	415	82.3%
Black/African American	50	9.9%
Asian American	33	6.5%
More than 1 Race Reported	3	0.6%
Native Hawaiian/Other Pacific Islander	2	0.4%
American Indian/Alaskan Native	1	0.2%
Missing	176	

Patient mean age was 55 years, and 60.4% of patients (n = 411) were female. Mean patient BMI (n = 521) was 29. Physicians reported that 16.5% of patients (n = 90) were current tobacco users and 10.6% of patients (n = 72) had current depression.

Almost all patients (91.8%, n = 624) had at least one service ordered or provided, including exams, screenings, laboratory tests, imaging, procedures, treatments, health education, or counseling. More than one quarter of physicians (26.3%, n = 179) reported having one or more exams ordered or provided. Almost one in five patients (18.5%, n = 126) had some type of imaging ordered or provided, including an x-ray for 7.2% of patients (n = 49), CT scan for 4.9% of patients (n = 33), or magnetic resonance imaging for 1.3% of patients (n = 9).

One or more write-in procedures were reported for 43.4% of patients (n = 295), for a total of 486 write-in procedures. Procedures included "other microscopic examination of blood" (17.5%, n = 85), upper endoscopy (13.8%, n = 67), "other consultation" (10.1%, n = 49), and general physical examination (3.5%, n = 17).

Of prescription and non-prescription medications reported, antacids were ordered or provided for 3.8% of patients (n = 26). Of the acid suppression medications, PPIs (41.3%, n = 281) were ordered or provided more often than H2 antagonists (7.9%, n = 54). TCAs were ordered or provided for 1.8% of patients (n = 12), and GI stimulants/prokinetics were ordered or provided for 1.6% of patients (n = 11). Psychotherapy was ordered or provided for 0.6% of patients (n = 4).

Noninvasive *H. pylori* testing was ordered or provided for 2.9% of patients (n = 20). *H. pylori* eradication therapy was given for 1.6% of patients (n = 11). Any EGD/upper endoscopy was ordered or provided for 12.8% of patients (n = 87; Table 4).

Table 4. Management provided.

	Frequency	Percent
Medications (Prescription and Non-Prescription)		
Proton Pump Inhibitors (PPIs)	281	41.3%
H2 Antagonists	54	7.9%
Antacids	26	3.8%
Tricyclic Antidepressants (TCA)	12	1.8%
GI Stimulants/Prokinetics	11	1.6%
***H. pylori* Testing or Treatment**		
Noninvasive *H. pylori* Test	20	2.9%
H. pylori Eradication Therapy	11	1.6%
EGD/Upper Endoscopy		
EGD/Upper Endoscopy	87	12.8%

When adherence was defined as provision of any component of the 2005 ACG dyspepsia guidelines, providers were considered adherent for 49.7% (n = 338) of patient visits. When adherence was defined as provision of any component of the 2017 ACG/CAG dyspepsia guidelines, providers were considered adherent for 51.0% (n = 347) of patient visits (Table 5). Addition of H2 antagonists for acceptable acid suppression raised adherence to 54.1% of patient visits (n = 368) for the 2005 ACG guidelines and 55.4% of patient visits (n = 377) for the 2017 ACG/CAG guidelines.

Table 5. Guideline adherence.

	Frequency	Percent
2005 ACG Guideline Criteria		
Total Adherence from 2012 through 2015	338	49.7%
Adherence in 2012	95	45.9%
Adherence in 2013	152	53.1%
Adherence in 2014	67	52.8%
Adherence in 2015	24	40.0%
2017 ACG/CAG Guideline Criteria		
Total Adherence from 2012 through 2015	347	51.0%
Adherence in 2012	95	45.9%
Adherence in 2013	154	53.8%
Adherence in 2014	72	56.7%
Adherence in 2015	26	43.3%

DISCUSSION

The prevalence of dyspepsia in this study was 0.26% (n = 680). A prior study suggested the prevalence of gastritis/dyspepsia to be 1.73% among adults.[17] The lower prevalence of dyspepsia within this study may be due to the strict inclusion criteria. It is likely that some patients presenting with dyspepsia were not reported as such by physicians during the patient record interview, and instead another reason for visit or diagnosis was used, such as upper abdominal pain (ICD-9-CM code 1545.3 upper abdominal pain, cramps, spasms) or diagnosis of gastric ulcer (ICD-9-CM code 531 Gastric Ulcer). The code for upper abdominal pain was not used for inclusion criteria in this study, as it encompasses more than just epigastric pain and likely would have overestimated the prevalence of dyspeptic patients within the study sample. Likewise, more specific diagnoses, such as gastric ulcers or gastrointestinal malignancy, were not used for inclusion criteria in this study, as they are considered underlying causes of dyspepsia identified on EGD which may require separate therapy.[18,19]

Diagnosis of *H. pylori* infection was used for inclusion criteria in this study, as the 2007 ACG Guideline on the Management of *Helicobacter pylori* Infection recommended diagnosis and treatment for select patients with uninvestigated dyspepsia.[16] Although diagnosis of *H. pylori* is indicated for reasons other than dyspepsia (e.g., peptic ulcer disease, gastric mucosa associated lymphoid tissue or MALT lymphoma), the diagnosis of *H. pylori* was used to identify a small proportion (13.1%) of the study sample and is unlikely to have a large impact on the results.[16] The diagnosis of GERD was used for exclusion, as GERD is considered a different diagnosis for patients presenting mainly with heartburn or acid regurgitation, rather than dominant epigastric discomfort or pain as in dyspepsia.[9]

The current study suggested dyspepsia to be more common among women. Uninvestigated dyspepsia may be more common among women, with a suggested global prevalence of 25.3% in women compared to 21.9% among men.[2] Patient mean age in this study was 55 years, which is slightly older than the mean ages of 47 years and 50 years of two other studies of patients with dyspepsia.[8,20]

In the current study, 18.5% of patients (n = 126) were ordered or provided an imaging service. A study of patients with persistent dyspepsia suggested that 87.1% of patients had received abdominal imaging, and the most frequent modalities were CT and ultrasound.[21] The lower frequency of imaging use in the current study could indicate a decreasing trend as study data were obtained from more recent years, although history of prior or later imaging services provided to patients in this study was not obtainable.

The current study suggested that PPIs were prescribed more often than H2 antagonists. Physician concern about adverse effects of PPI therapy have been suggested, with 52% of internal medicine physicians self-reporting they sometimes or often changed a patient's prescription from PPI therapy to H2 antagonists.[22] A prior study suggested H2 antagonists were prescribed more frequently than PPIs in patients with uninvestigated dyspepsia (88.1% versus 47.4%, respectively).[13] However, the current study's findings were consistent with guideline recommendations, and this increased usage of PPIs over H2 antagonists for acid suppression therapy may indicate guideline adherence in this area.[1,9]

Half of patients with dyspepsia in this study received at least one treatment, diagnostic test, or exam recommended by either the 2005 ACG or 2017 ACG/CAG guidelines. This percentage of patients receiving care specified within dyspepsia management guidelines was suboptimal and indicated low physician adherence to dyspepsia management guidelines. Furthermore, there was minimal difference between the percent of visits adherent to the 2005 compared to the 2017 guidelines, indicating the additional therapies considered adherent by the 2017 guidelines were not utilized frequently in the years preceding the release of the 2017 guidelines. This limited difference in adherence also clarified that most visits considered non-adherent with the 2005 guidelines were not provided the more novel therapies considered to be adherent by the 2017 guidelines.

Physicians may be non-adherent due to lack of knowledge of guidelines. A review of guideline adherence barriers suggested physicians were more likely to be unfamiliar with guideline content than unaware of their existence.[23] Therefore, dissemination of the 2017 ACG/CAG guidelines with its management algorithm to physicians working in ambulatory care settings may improve knowledge and adherence to dyspepsia management guidelines. However, this strategy alone may not be sufficient to raise adherence levels, as passive dissemination of guidelines has been suggested to be ineffective for guideline implementation.[24] Further interventions, including workshops, handouts, and reminders, may be beneficial as they have been suggested to lower drug costs of dyspepsia without increasing endoscopy use.[25]

Increased monitoring of guideline adherence in clinical practices may be beneficial. Notifying providers when their endoscopy referral for dyspepsia management was not adherent with guidelines was suggested to increase adherence rates from 55% to 75%.[26] Less targeted approaches to increase physician acceptance and adherence to all clinical guidelines may be useful, as one study suggested clinical practice guidelines only have a large or very large effect on how less than 25% of physicians practice medicine.[27] Both targeted and general approaches

to increase guideline adherence may be necessary to ensure evidence-based medicine is practiced.

There were several limitations of this study. NAMCS is a voluntary survey of physicians. As a result, data may be influenced by response and/or recall bias. There was also variability in the number of records meeting inclusion/exclusion criteria per year. The highest number of patient records meeting criteria for this study was 286 records in 2013 and the lowest number was 60 in 2015. The lack of consistency in the total number of patient records available per year from the NAMCS database may have led to increased variability in the data. However, the percentage of records determined to be adherent to guidelines in this study remained low in each year, ranging from 40.0% to 53.1% for the 2005 guidelines and from 43.3% to 56.7% for the 2017 guidelines.

The lack of available CPT codes, the broadness of the ICD-9-CM codes, and the variability in the checkbox items included in the survey from year to year made capturing accurate and consistent data difficult. For example, upper gastrointestinal endoscopy/EGD was included as a checkbox item for examinations/screenings ordered or provided for survey years 2014 and 2015, but not for years 2012 or 2013. Furthermore, appropriateness of the use of treatments or tests for each patient based upon specific indications (such as presence of alarm features, risk of malignancy, or previous treatment or test results) could not be assessed in this cross-sectional study. Additionally, some patients may have not desired or had counter-indications to receiving the guideline recommended test or treatment, making non-adherence acceptable in these specific situations. Therefore, adherence may have been over or underestimated, as the specific order and situational appropriateness of guideline provision could not be assessed.

Despite the challenges of using NAMCS data, the survey captured national, systematic data on ambulatory care practices within the U.S. It is a valuable source of information about clinical practices of U.S. physicians.

CONCLUSIONS

Provider adherence with both the 2005 ACG and the 2017 ACG/CAG dyspepsia management guidelines was determined to be low in this study, with 50% of patients receiving a recommended test or treatment. Physician adherence must increase to evidence-based management of patients with dyspepsia and utilize healthcare resources appropriately and efficiently.

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Keywords: dyspepsia, gastroenterology, guideline adherence, patient care management, practice guidelines as topic

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Changes in Family Physicians' Perceptions of Electronic Cigarettes in Tobacco Use Counseling Between 2016 and 2019

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Received July 10, 2020; Accepted for publication Sept. 10, 2020; Published online Dec. 11, 2020
https://doi.org/10.17161/kjm.vol13.13877

ABSTRACT

Introduction. Given the recent reports of e-cigarette, or vaping, product use-associated lung injury (EVALI) and harm of e-cigarettes, the authors evaluated changes in the use and perception of e-cigarettes as tobacco use cessation tools in 2019 relative to 2016. The authors also evaluated the sources family physicians most commonly use to receive information regarding e-cigarettes.

Methods. A cross-sectional online survey of 248 community family physicians in Kansas was conducted from October 2019 to December 2019. An 11-item questionnaire measured the participants' perceptions of recommending e-cigarettes to patients for tobacco cessation. A mixed method approach was used to collect, analyze, and interpret the data. Standard descriptive statistics, Likelihood-Ratio/Fisher's exact tests, and immersion-crystallization methods were used to analyze the data.

Results. The response rate was 59.3% (147/248). The proportion of the family physicians who did not recommend e-cigarettes for tobacco use cessation was significantly higher in 2019 than in 2016 (86% vs. 82%; χ^2 [1, n = 261] = 12.31; p < 0.01). Several reasons regarding respondents' perceptions of e-cigarettes as tobacco use cessation tools were reported. The medical literature and news media were the top sources where family physicians accessed e-cigarettes information.

Conclusion. Most family physicians did not recommend e-cigarettes for tobacco cessation. Opinions regarding the efficacy and safety of e-cigarettes were influenced by information sources. Future, larger studies would be beneficial to further determine family physicians' beliefs and practices regarding e-cigarettes as tobacco use cessation products. ***Kans J Med 2020;13:311-317***

INTRODUCTION

In August 2019, the U.S. Centers for Disease Control and Prevention (CDC) reported that it was investigating more than 215 cases of severe lung illness and the possible link with electronic cigarette (e-cigarette) products in 25 states.[1,2] Subsequently, several case series reported lung injury associated with vaping ranging from pneumonia to acute respiratory distress syndrome requiring mechanical ventilation.[3] A reported 2,807 e-cigarette, or vaping, product use-associated lung injury (EVALI)-related cases were reported from all 50 states, as well as the District of Columbia, and two U.S. territories (Puerto Rico and U.S. Virgin Islands), with 68 deaths.[4] Publications in the lay press have called attention to the impact of vaping on teens and young adults, increasing public awareness of vaping-related lung illnesses.[5-8]

As reports of harm associated with vaping rise and as efficacy of tobacco use cessation with e-cigarettes remains uncertain, the debate on the use of e-cigarettes as a tobacco use cessation strategy continues.[9-11] This study was conducted to evaluate if the 2019 outbreak of EVALI and resultant medical and media reports were associated with a change in family physicians' perceptions of e-cigarettes as tobacco use cessation tools. Family physicians' perception of e-cigarettes for tobacco use cessation were first reported in 2017.[12] Here, results of a follow-up 2019 survey are presented to evaluate changes in the perception of e-cigarettes as tobacco use cessation products with comparison to 2016 findings. The sources family physicians most commonly used to receive information regarding e-cigarettes also were evaluated.

METHODS

Study Design. This study was a cross-sectional survey of Kansas family physicians in active practice. The 2019 survey used methods similar to those of the study published in 2017,[12] a mixed methods approach to collect, analyze, and interpret the data.[13] The quantitative approach allowed the authors to obtain value-free and objective insights into the respondents' opinions about e-cigarettes, while the qualitative approach allowed for an in-depth understanding of those insights. Community-based family physicians were surveyed as well as faculty and resident physicians of the three family medicine residencies sponsored by the University of Kansas School of Medicine-Wichita (KUSM-W) Department of Family and Community Medicine (DFCM). The questionnaire focused on physician perceptions of recommending e-cigarettes for tobacco cessation. The KUSM-W Institutional Review Board granted exemption for the study as non-human subject research.

Study Instrument and Data Collection Process. An 11-item questionnaire (Appendix A) similar to what was used in the 2017 study, measured family physicians' perceptions of recommending e-cigarettes to patients for tobacco cessation.[12] The survey questionnaire was hosted in SurveyMonkey®, a secure web-based survey system. A generated link to the survey was sent via email to potential participants. The DFCM used an email system called FM-RADIO (Family Medicine Research and Data Information Office) as a survey collection tool. The FM-RADIO is an electronic practice-based research network comprised of family physicians throughout the State of Kansas who are KUSM-W Family Medicine Residency program graduates, actively practicing family physician non-graduates, faculty physicians, and resident physicians. The link initially was sent to 248 community physicians, faculty physicians, and resident physicians who were on the FM RADIO list. Two reminders subsequently were sent to those who had not completed the survey. The data were collected from October 2019 to December 2019.

Data Analyses. Standard descriptive statistics were used to create a demographic profile of the respondents. Associations between the variables, as well as comparison between the proportion of family

physicians who recommended e-cigarettes as tobacco use cessation products in 2016 and 2019, were evaluated using a Likelihood-Ratio test. The Likelihood-Ratio test evaluated the relationship between the family physicians' decisions to recommend e-cigarettes as tobacco use cessation products and the sources where they commonly obtained information regarding e-cigarettes. The respondents' perceived effectiveness of e-cigarettes was clustered into three groups (ineffective [combination of very ineffective and ineffective], neither ineffective nor effective, and effective [combination of very effective and effective]) and compared between the two time periods (2016 and 2019) using a Fisher's exact test. The Fisher's exact test was used in cases where the expected numbers were small.

The study team used an immersion-crystallization approach[13-15] to analyze the content of respondents' qualitative data (open-ended responses) individually and in a group meeting. Immersion-crystallization is a process where researchers examine collected data in detail and periodically suspend the immersion process to reflect on emerging findings until consistent themes are identified.[13,15] This multidisciplinary team was composed of a health psychologist (SO-D), two family physicians (RK, JW), a behavioral scientist (RN), and a family medicine resident (KG). All quantitative analyses were performed with a two-sided alpha of 0.05 using IBM SPSS (Statistical Package for the Social Sciences) package, version 26.

RESULTS

Participant Characteristics. Of the 248 potential participants, data were collected from 147, a 59.3% response rate. As shown in Table 1, the demographic characteristics of the 2019 respondents were statistically different from those of the 2016 survey in age ($p = 0.007$), career status ($p < 0.001$), years in practice ($p = 0.004$), and years as a full-time faculty physician ($p = 0.040$). There was no statistical difference between the two cohorts in terms of sex.

Quantitative Results. The proportion of the family physicians who did not recommend e-cigarettes for tobacco use cessation was significantly higher in 2019 than in 2016 (86% vs. 82%; χ^2 [1, n = 261] = 12.31; $p < 0.01$), and respondents listed several reasons for their decisions. The physicians' career status (community-based physicians, full-time faculty physicians, and resident-physicians) and decision to recommend e-cigarettes (yes or no) were found to be not significantly related (χ^2 [2, n = 140] = 2.52; $p > 0.05$). The percentages of community-based physicians, full-time faculty physicians, and resident-physicians were 87.3%, 77.4%, and 89.9%, respectively.

Family physicians were asked where they most commonly received information about adverse effects of e-cigarettes. Of 137 respondents, 45.3% received information from medical literature, 37.2% from news media, 8.0% from colleagues, 3.6% from social media, and 5.8% from other sources, including the American Academy of Family Physicians (AAFP) SmartBrief e-newsletter, AAFP and/or the American Medical Association (AMA) newsletters, and the U.S. Centers for Disease Control and Prevention (CDC) website. These sources of information were grouped into three clusters (medical literature, news media, and all other sources [combination of colleagues, social media, other professional organizations]). The reason for the grouping of all other sources was the relatively low number of respondents who used these individual methods of accessing information.

Table 1. Demographic profile of participants.

Characteristics	2019 Respondents (N = 147)	2016 Respondents (N = 117)	p value
Sex, no. (%)			
Male	77 (55.4)	57 (53.3)	
Female	62 (44.6)	50 (46.7)	
Missing*	8	10	
Age, years			0.007
Range	25 to ≥ 65	25 to ≥ 65	
18 - 24	0 (0)	0 (0)	
25 - 34	50 (36.0)	60 (56.1)	
35 - 44	30 (21.6)	23 (21.5)	
45 - 54	24 (17.3)	13 (12.2)	
55 - 64	18 (12.9)	7 (6.5)	
≥ 65	17 (12.2)	4 (3.7)	
Missing*	8	10	
Career status, no. (%)			< 0.001
Practicing family physician	71 (50.7)	27 (25.2)	
Full-time faculty	31 (22.2)	25 (23.4)	
Resident-physician	36 (25.7)	55 (51.4)	
Fellow	0	0	
Other	2 (1.4)	0	
Missing*	7	10	
Years in practice, no.			
Range	5 months to 44 years	3 to 38 years	
Mean (SD)	18 (12.4)	21 (10.9)	0.004
Years as a full-time faculty, no.			
Range	4 months to 31 years	2 months to 22 years	
Mean (SD)	13 (10.4)	8.2 (6.6)	0.040
Medical trainees, no. (%)			
First-year residents	10 (27.8)	18 (32.7)	
Second-year residents	12 (33.3)	20 (36.4)	
Third-year residents	14 (38.9)	17 (30.9)	

SD = Standard deviation
*The number of family physicians who completed the survey but did not provide an answer to this specific question. Missing responses were excluded from the total before percentages were calculated.

A Likelihood-Ratio test was conducted to evaluate the relationship between the family physicians' decisions to recommend e-cigarettes as tobacco use cessation products and the sources where they commonly obtained information regarding e-cigarettes. The variables were correlated significantly (χ^2 [2, n = 137] = 6.8; p = 0.012; Cramer's V = 0.36; Table 2a). Follow-up pairwise comparisons were conducted to evaluate the differences among the groups. Holmes sequential Bonferroni method was used to control for Type I error at 0.05 across all the comparisons. Significant pairwise difference was found between medical literature and news media (Table 2b). Family physicians were less likely to recommend e-cigarettes as tobacco use cessation products if they commonly received information regarding e-cigarettes from the medical literature compared to the news media.

To determine if there was a change between 2016 and 2019 respondents' perceived effectiveness of e-cigarettes as tobacco use cessation products, comparisons among the three effectiveness groups were conducted using a Fisher's exact test. The results revealed statistically significant differences among the groups (Figure 1). There was a reduction in the proportion (70.8% vs. 41.1%) of respondents who perceived e-cigarettes as an ineffective tobacco use cessation tool from 2016 to 2019. Nearly 80% of the 2019 respondents reported that e-cigarettes were either ineffective or were ambivalent about e-cigarettes as an effective tobacco cessation tool.

Qualitative Results: Family Physicians who Recommended E-cigarettes. Of the 247 respondents in the 2019 survey, 13.6% reported they recommended e-cigarettes for tobacco use cessation. Two major themes with three sub-themes emerged as reasons: e-cigarettes serve as tobacco use cessation products and e-cigarettes are the lesser of two evils compared to combustible cigarettes (Table 3).

Qualitative Results: Family Physicians who did not Recommend E-cigarettes. Just over 86% of the 247 family physicians in the 2019 survey did not recommend e-cigarettes for tobacco use cessation. Six themes emerged from the analyses: lack of data to support effectiveness of e-cigarettes, e-cigarettes are just as bad as combustible cigarettes, e-cigarettes are not regulated or not approved by the United States Food and Drug Administration (FDA), better options are available, concerns about safety of e-cigarettes, and other reasons (Table 4).

DISCUSSION

Our study demonstrated a statistically significant increasing trend in recommending against e-cigarette use for tobacco use cessation among family physicians. Compared to 2016, family physicians in the 2019 survey were more likely to recommend against e-cigarettes for tobacco use cessation. Reasons against recommending e-cigarettes included lack of evidence regarding both efficacy and safety, as well as increased concern of harms. These trends are consistent with the 2019 outbreak of EVALI and recommendations from government and professional organizations, including the CDC and AAFP, to continue to recommend evidence-based tobacco use cessation counseling methods and FDA-approved tobacco use cessation products over e-cigarettes.

In anticipation of a change in family physicians' recommendations due to recent safety concerns, physicians were surveyed regarding their sources of information about e-cigarettes. Physicians who recommended against e-cigarettes were more likely to obtain information from the medical literature compared to news media, whereas physicians who recommended e-cigarettes were more likely to obtain information from the news media. Likewise, several major medical journals published case series and reports regarding EVALI.[16-19] One possible reason for the variance in recommending e-cigarettes by information from medical literature may have been either more knowledge or concern regarding the potential harms of e-cigarettes.

Ambiguity in opinions regarding e-cigarette efficacy was apparent in our study and was supported by the conflicting current state of evidence. Interestingly, our results showed that family physicians were ambivalent about e-cigarettes as an effective tobacco cessation tool, and the majority did not recommend them. Furthermore, while more than one-third of physicians who did not recommend e-cigarettes reported a lack of supporting evidence about their effectiveness as an underlying reason, nearly one-quarter of physicians who recommended e-cigarettes noted efficacy as a reason they supported use. These differences in opinion are mirrored in the medical literature and major organizations' recommendations. For example, a 2016 Cochrane review found limited, low quality evidence that e-cigarettes are effective for tobacco use cessation, but not more than nicotine replacement.[20] More recent randomized controlled trials (RCTs) have shown contradictory results.

While a 2018 RCT (N = 6,131) did not find e-cigarettes to be more effective than tobacco use cessation counseling or nicotine replacement,[21] a 2019 RCT (N = 844) showed e-cigarettes to be more effective than nicotine replacement for tobacco use cessation.[22] However, among patients who quit tobacco, 80% (63 of 79) who used e-cigarettes were using them still at 52 weeks compared to only 9% (4 of 44) of the nicotine replacement group.[2]

Additional reasons for not recommending e-cigarettes included the belief that e-cigarettes are "just as bad" as combustible cigarettes. For example, one physician noted that "they [e-cigarettes] are not any safer. We do not know what is in them." Physicians also were concerned about harmful additives and lack of regulation by the FDA. Others reported the availability of better options, such as nicotine replacement, bupropion, and tobacco cessation counseling, which are consistent with recommendations from the AAFP and CDC.

The majority of physicians who recommended e-cigarettes cited the ability to titrate down, or taper nicotine as a reason for e-cigarettes as a cessation tool. This was a new finding compared to the 2016 study. While using e-cigarettes may be seen as a way to taper off of nicotine, the evidence noted above suggests the contrary.[22,23]Additional reasons for recommending e-cigarettes were similar to the 2016 study, which included the belief that they are the "lesser of two evils" and a "second-line option" if the patient requests it or declines other options. E-cigarettes often are marketed as a healthier alternative to tobacco.[24,25] While limited evidence suggested a reduction in exposure to tobacco-related carcinogens and toxins among e-cigarette users, e-cigarettes also are known to contain harmful toxins, including flavoring associated with lung injury, volatile organic compounds, and carcinogens.[26]

Table 2a. Relationship of respondents' common sources of information regarding adverse effects of e-cigarettes compared with e-cigarettes recommendation, 2019.

	Recommending E-cigarettes					
Measures	**Yes**	**No**	**Total**	**Pearson χ^2**	**p value**	**Cramer's *V***
Sources of information, no. (%)				8.60	0.012	0.36
Medical literature	8 (12.9)	54 (87.1)	62 (100)			
News media	11 (21.6)	40 (78.4)	51 (100)			
Other sources	5 (20.8)	19 (19.2)	24 (100)			
Total	24 (17.5)	113 (82.5)	137 (100)			

Table 2b. Results for pairwise comparison using the Holm Sequential Bonferroni method, 2019.

Comparisons	Pearson $\chi 2$	p value (α)	Cramer's V
Medical literature vs news media	8.97*	0.011 (0.017)	0.38
Medical literature vs other sources	3.26	0.037 (0.025)	0.13
News media vs other sources	1.64	0.16 (0.050)	0.18

*p value ≤ α

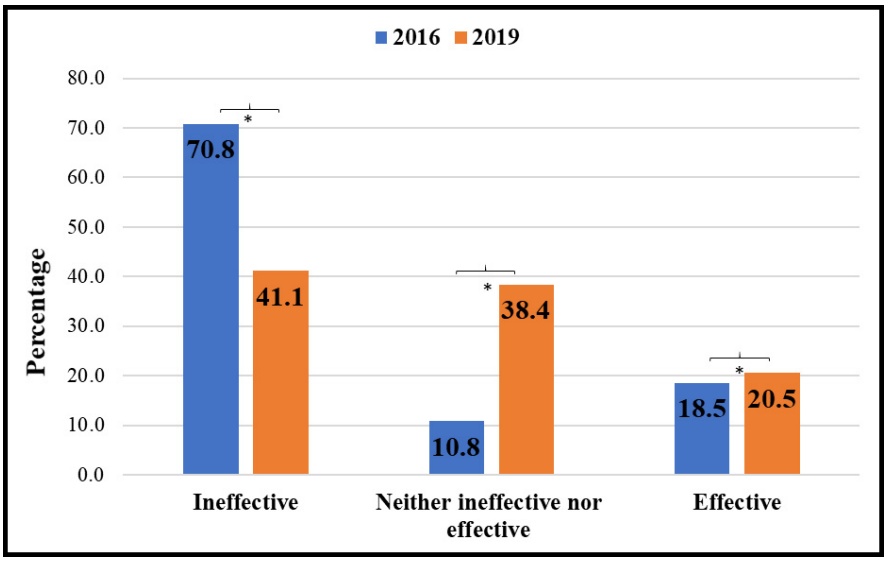

Figure 1. Family physicians' perceived effectiveness of electronic cigarettes in 2019 compared with 2016.
*Statistical difference

Table 3. Open-ended comments on reasons family physicians recommended e-cigarettes for tobacco use cessation, 2019 (Responses = 37).

Themes	Percentage of Responses	Quotes from Participants
E-cigarettes are tobacco use cessation products		
Ability to titrate nicotine	62%	"It can be a useful way to taper nicotine."
		"Provides an alternative until patient is ready to get off nicotine."
Effective smoking cessation products	23%	" The evidence supports increase success."
		"Improve rates of smoking cessation. If used as recommended without flavor packs or other additives."
Good second line option for smoking cessation	15%	"Yes, but only if patients ask about it as an option to quit and with the caveat that it should only be used as a cessation tool but not a substitute."
		"If the patient requests it. I offer it more if it's the only option the patient will consider."
Less risk/lesser of two evils	30%	[I] "generally believe they are less bad then real cigarettes."
		"To reduce other family members exposure to secondhand smoke and as a way to taper nicotine."

Table 4. Open-ended comments on reasons family physicians did not recommend e-cigarettes for tobacco use cessation, 2019 (Responses = 153).

Themes	Percentage of Responses	Quotes for Participants
Lack of data to support effectiveness of e-cigarettes	35%	"Studies that show benefit are limited and there is no long-term data with effects of the device."
		"Still very poor study data, likely still exposure to harmful chemicals."
E-cigarettes are just as bad as combustible cigarettes	30%	"I feel they are just as bad for an individual's health and just as addictive as cigarettes."
		"They are not any safer. We do not know what is in them."
Lack of regulation/Not FDA approved	11%	"Unregulated product with unknown long-term effects."
		"Flavor contents unregulated by the FDA, still a tobacco product."
Availability of better options	10%	[I] "recommend other forms of treatment for nicotine withdrawal that don't mimic the act of smoking."
		"Little experience with e-cigarettes. Prefer to use other recommended resources for smoking cessation such as NRT, Chantix, or bupropion, as well as Yes-800-QUIT-NOW or Behavioral Health if interested."
Safety concerns about the use of e-cigarettes	10%	"Recent evidence and case reports of lung disease and deaths associated with e-cigs."
		"Severe related lung injury documented recently and uncertain long-term side effect profile."
Other reasons	4%	"It's stupid. If you want to quit smoking why recommend another smoking object to put more toxins. Why not just say use marijuana to quit cigarettes. Same logic. Both stupid."
		"I allow patients to use them to assist with quitting, but I don't suggest it to them."

The 2019 survey had a higher proportion of older and currently practicing physicians compared to the 2016 survey, which included a higher proportion of resident physician respondents. In the 2016 study, being younger and a resident physician were associated with opposing e-cigarette use compared to more experienced community physicians. Despite having a greater proportion of community physicians in the 2019 study, there was an increasing trend to recommend against e-cigarettes for tobacco use cessation. This may be due to new evidence of significant potential harm from e-cigarettes including EVALI, as well as lack of consistent, high quality evidence that e-cigarettes are an effective tobacco cessation product. Additionally, it could be that resident physician respondents in the 2016 survey were now community physicians, thus opinions have not significantly changed.

Our study had several limitations. This survey presented a snapshot of family physicians' subjective responses about vaping. The results were limited to those community family physicians who were in active practice, as well as faculty and resident physicians of the three family medicine residencies sponsored by the KUSM-W at the time of the study who chose to respond to the survey. Although several family physicians in Kansas were on the KUSM-W DFCM FM-RADIO list, the opinion of those who were not on the list could have changed the results of the study. Finally, due to the small sample size of our study, caution should be exercised in generalizing results to the larger medical community. Future, larger studies would be beneficial to further determine physicians' beliefs and practices regarding e-cigarettes as a tobacco use cessation tool.

CONCLUSIONS

Our study suggested that the majority of family physicians did not recommend e-cigarettes for tobacco cessation. There were varied opinions regarding efficacy and safety of e-cigarettes. These opinions were influenced by information source. Given recent safety concerns and lack of consistent evidence regarding efficacy of e-cigarettes, family physicians should consider recommending only current evidence-based smoking cessation methods to patients.

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Keywords: electronic cigarettes, family physician, lung injury, tobacco use cessation, Kansas

The following set of questions seeks to assess your opinion regarding recommending electronic cigarettes to patients who smoke.

1. Do you recommend electronic cigarettes for smoking cessation?
   a. Yes
   b. No
   Why or why not? ____

2. Would you recommend electronic cigarettes to a patient who cannot, or does not, want to stop smoking?
   a. Yes
   b. No
   Why or why not? ____

3. Have you ever recommended electronic cigarettes for smoking cessation?
   a. Yes
   b. No
   Why or why not? ____

4. In your opinion, how effective are electronic cigarettes in helping smokers to quit?
   a. Very effective
   b. Effective
   c. Neither effective nor ineffective
   d. Ineffective
   e. Very ineffective

5. Where do you most commonly receive information about adverse effects of electronic cigarettes?
   a. Medical literature
   b. News Media
   c. Social Media
   d. Colleagues
   e. Other (please specify) ____

6. What is your current age? (Please select the range into which your age falls)
   a. 18 - 24 years
   b. 25 - 34 years
   c. 35 - 44 years
   d. 45 - 54 years
   e. 55 - 64 years
   f. ≥ 65 years

7. What is your Gender? (Please select one)
   a. Male
   b. Female
   c. Other (please specify) ____

8. I'm a...
   a. Full time practicing family physician
   b. Full time faculty
   c. Resident-physician
   d. Fellow
   e. Other (please specify) ____

9. What is the number of years since you graduated from residency? ____

10. How long have you been a faculty physician? ____

11. What is your current year in residency?
    a. PGY 1
    b. PGY 2
    c. PGY 3

Thank you for participating!

KANSAS JOURNAL of MEDICINE

E-cigarette Use and Risk Behaviors among Lesbian, Gay, Bisexual, and Transgender Adults: The Behavioral Risk Factor Surveillance System (BRFSS) Survey

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Received July 8, 2020; Accepted for publication Sept. 14, 2020; Published online Dec. 11, 2020
https://doi.org/10.17161/kjm.vol13.13861

ABSTRACT

Introduction. The prevalence of e-cigarette use among lesbian, gay, bisexual, and transgender (LGBT) individuals and its association with risk behaviors was studied.

Methods. Using data from the Behavioral Risk Factor Surveillance System (BRFSS) survey, self-reported sexual orientation, e-cigarette use, cigarettes, marijuana, smokeless tobacco, and high-risk behavior (using non-prescribed drugs, treatment for sexually transmitted disease, or receiving monetary or drug compensation in exchange for sex in the previous year) were assessed. Multivariable-adjusted logistic regression models were used to study the association between LGBT and risk behaviors.

Results. The prevalence of e-cigarette use among LGBT adults was 13%, nearly twice that of heterosexual adults. LGBT adults were more likely [Odds Ratio (95% Confidence Interval)] to report current use of e-cigarettes 1.84 (1.64, 2.06), cigarettes 1.61 (1.49, 1.73), marijuana 2.37 (1.99, 2.82), and high-risk behavior 3.69 (3.40, 4.01) compared to heterosexual adults. Results for smokeless tobacco were not significant.

Conclusion. There are disparities in e-cigarette and other risk behaviors among LGBT adults, which may increase risk of adverse health effects in this vulnerable population. ***Kans J Med 2020;13:318-321***

INTRODUCTION

The past few decades have witnessed an overall decline in tobacco smoking rates due to efforts aimed at improving public awareness on the dangers of cigarette smoking and the health benefits of smoking cessation. On the other hand, there has been an increase in e-cigarette use and other vaping-related products. This likely is related, in part, to marketing strategies advertising e-cigarettes as safer alternatives to conventional tobacco products, often targeting vulnerable populations. The increase in e-cigarette consumption has been linked to serious cardiopulmonary health effects,[1-6] though there are no epidemiologic data to support a higher risk of long-term events with these products.

Cigarette smoking is higher among LGBT (lesbian, gay, bisexual, and transgender) populations compared with heterosexual adults.[7] LGBT represent a minority group in the U.S., and this population has been shown to have a disproportionately higher risk of adverse outcomes.[8] These disparities could be explained by risk behaviors that may be more prevalent among sexual minority groups compared to the general population.[9,10] This underscores the importance of screening for such behaviors and to develop interventions to mitigate possible health effects.

The present study investigated the association between sexual orientation and risk behaviors including tobacco use patterns (cigarette, e-cigarette, smokeless tobacco), marijuana, and high-risk sexual behaviors in a nationally representative U.S. sample. Stratified analyses were performed by age and gender to determine whether certain subgroups of the LGBT population may be particularly at high risk of such risk behaviors. Lastly, temporal trends in the prevalence of these behaviors were evaluated.

METHODS

Study Population and Study Design. The Behavioral Risk Factor Surveillance System (BRFSS) survey is established by the Centers for Disease Control and Prevention. It is a nationwide telephone-based questionnaire that is administered to a random sample of U.S. adult residents. The BRFSS survey aims to evaluate health-related risk behaviors, chronic health conditions, and the use of preventive services in a representative sample of U.S. adults. The survey is conducted in all 50 states, the District of Columbia, and the three U.S. territories. This makes BRFSS the largest telephone-based survey in the world. Cross-sectional data from BRFSS surveys conducted in 2016, 2017, and 2018 (n = 1,348,091) were utilized. The 2018 dataset included participants interviewed in the year 2019, therefore, trends up until year 2019 were evaluated. Given that BRFSS is a publicly available dataset, these analyses did not require Institutional Review Board approval.

Definition of LGBT. Complete information on LGBT status was available for 510,398 participants. LGBT status was self-reported and defined as participants identifying themselves as being lesbian, gay, bisexual, or transgender. Participants answering "Yes" to the question, "Do you consider yourself to be straight?", were classified as heterosexual.

Definition of Risk Behaviors. E-cigarette status was ascertained if participants reported ever using e-cigarette or other electronic vaping products. Current users were defined as participants reporting currently using these products every day or some days. Cigarette smokers were identified as participants who reported having smoked

at least 100 cigarettes in their lifetime. Ever smokers were classified as current or former depending on whether they currently smoked cigarettes every day or some days. Smokeless tobacco use was classified as participants reporting yes to the questions assessing current use of chewing tobacco, snuff, or snus every day or some days. Marijuana use was classified as participants reporting use of marijuana or hashish at least one day in the previous 30 days. High-risk behavior was defined if participants reported ever using non-prescribed drugs, were treated for sexually transmitted disease, or if they received monetary or drug compensation in exchange for sex in the previous year.

Statistical Analysis. BRFSS data were analyzed using survey weights as BRFSS employed design weighting and iterative proportional fitting to ensure adequate representation of the general U.S. population. The association between sexual orientation (LGBT vs. heterosexual) and risk behaviors was studied using weighted multivariable logistic regression models. Covariates adjusted for in this analysis included age, poverty level, education, race/ethnicity, marital status, and employment status. Results were stratified by age groups and gender.

Similar multivariable-adjusted logistic regression models were used to study the association between current e-cigarette use and other risk behaviors among LGBT subjects. Lastly, prevalence of these risk behaviors was examined between 2016 and 2019 and tested for significance using Pearson χ^2 statistic.

Analyses were conducted using Stata version 13.1 (StataCorp, College Station, Texas). All p-values were two-sided and $p < 0.05$ was considered statistically significant.

RESULTS

Among 510,398 participants, 4.8% (n = 20,011) reported being LGBT (53% were aged 18 - 34 years, 38% were men, 60% were White, 13% were Black, and 17% were Hispanic). Among LGBT subjects, the prevalence of current e-cigarette use was 13.0% (95% CI; 12.0%, 14.2%) versus 4.8% (4.6%, 4.9%) among heterosexuals. Other risk behaviors were also higher among LGBT subjects compared to heterosexuals (Table 1).

LGBT and Risk Behaviors. In multivariable-adjusted analyses, LGBT adults as compared to heterosexuals had higher odds (Odds Ratio (95% Confidence Interval)) of currently using e-cigarettes: 1.84 (1.64, 2.06), cigarettes: 1.61 (1.49, 1.73), as well as dual use of these products: 1.69 (1.47, 1.94). LGBT adults also had higher odds of using marijuana: 2.37 (1.99, 2.82) and engaging in high-risk behavior: 3.69 (3.40, 4.01) There was no significant association between LGBT and smokeless tobacco use (Table 2). Similar results were obtained in analyses stratified by age and gender (results not shown).

Current E-cigarette Use and Risk Behaviors among LGBT Subjects. Current e-cigarette use among LGBT subjects was significantly associated with higher odds of current cigarette smoking: 8.71 (6.82, 11.13), smokeless tobacco use: 2.51 (1.37, 4.59), and marijuana use: 6.02 (3.65, 9.94).

Temporal Trends in Risk Behaviors. In trend analyses, there was a significantly increasing prevalence of current e-cigarette use, current cigarette use, and high-risk behavior among LGBT subjects between the years 2016 and 2019 (Figure 1).

Table 1. Baseline characteristics of the study population by sexual orientation.*

	Heterosexual N = 490,387 (95%)	LGBT N = 20,011 (5%)
Age (years)		
18 - 34	66,715 (26)	7,206 (53)
35 - 44	54,521 (16)	2,699 (14)
45 - 54	78,112 (17)	3,146 (13)
55 - 64	110,332 (18)	3,487 (11)
≥ 65	180,707 (22)	3,653 (9)
Gender		
Men	162,742 (40)	7,269 (38)
Women	327,453 (60)	12,678 (62)
Race/ethnicity		
White	375,579 (64)	14,105 (60)
Black	40,186 (12)	1,667 (13)
Hispanic	31,705 (16)	1,895 (17)
Other	35,820 (8)	2,012 (10)
Education		
Less than high school	32,339 (13)	1,431 (13)
High school - some college	269,269 (60)	10,547 (61)
Greater than college	187,608 (28)	7,984 (26)
Marital status		
Married	253,888 (52)	5,896 (26)
Divorced/separated	80,639 (14)	2,921 (11)
Widowed	67,804 (8)	1,102 (3)
Single	85,694 (26)	9,975 (60)
Employment status		
Employed	236,472 (56)	11,095 (58)
Unemployed	84,461 (19)	4,070 (21)
Student	11,299 (5)	1,360 (11)
Retired	155,268 (20)	3,345 (9)
Income		
< $50,000	210,761 (43)	10,001 (50)
≥ $50,000	279,626 (57)	10,010 (50)
Current cigarette smoking status	69,132 (15)	4,571 (25)
Current e-cigarette use	14,041 (5)	1,456 (13)
Every day	4,903 (34)	489 (32)
Some days	9,138 (66)	967 (68)
Dual e-cigarette and cigarette use	7,571 (2)	781 (4)
Smokeless tobacco use	12,474 (2.9)	540 (3.3)
Marijuana at least once per month	4,968 (8)	741 (25)
High risk behavior	14,646 (5)	3,626 (24)

*Categorical variables are listed as counts (percentage).

Table 2. Multivariable-adjusted[φ] odds ratios (95% confidence interval) for the association of LGBT with risk behaviors.

	Question asked	Health factor definition	Heterosexual	LGBT	
				Unadjusted	Adjusted
Current e-cigarette use	Have you ever used an e-cigarette or other electronic vaping product, even just one time, in your entire life?	Current e-cigarette use	1 (ref)	2.97 (2.68, 3.29)	1.84 (1.64, 2.06)
Current cigarette use	Do you now smoke cigarettes every day, some days, or not at all?	Current cigarette use	1 (ref)	1.83 (1.71, 1.95)	1.61 (1.49, 1.73)
Dual e-cigarette and cigarette use	There was no question specifically pertaining to dual use in BRFSS.	Dual use	1 (ref)	2.41 (2.12, 2.75)	1.69 (1.47, 1.94)
Smokeless tobacco	Do you currently use chewing tobacco, snuff, or snus every day, some days, or not at all?	Yes	1 (ref)	1.17 (0.97, 1.39)	0.96 (0.98, 1.15)
Marijuana	During the past 30 days, on how many days did you use marijuana or hashish?	Yes	1 (ref)	3.80 (3.23, 4.48)	2.37 (1.99, 2.82)
High risk behavior	Have you injected any drug other than those prescribed for you in the past year? Have you been treated for a sexually transmitted disease or STD in the past year? Have you been given or received money or drugs in exchange for sex in the past year?	Yes	1 (ref)	6.13 (5.70, 6.60)	3.69 (3.40, 4.01)

[φ]Model is adjusted for age, race/ethnicity, poverty level, education, employment status, and marital status.

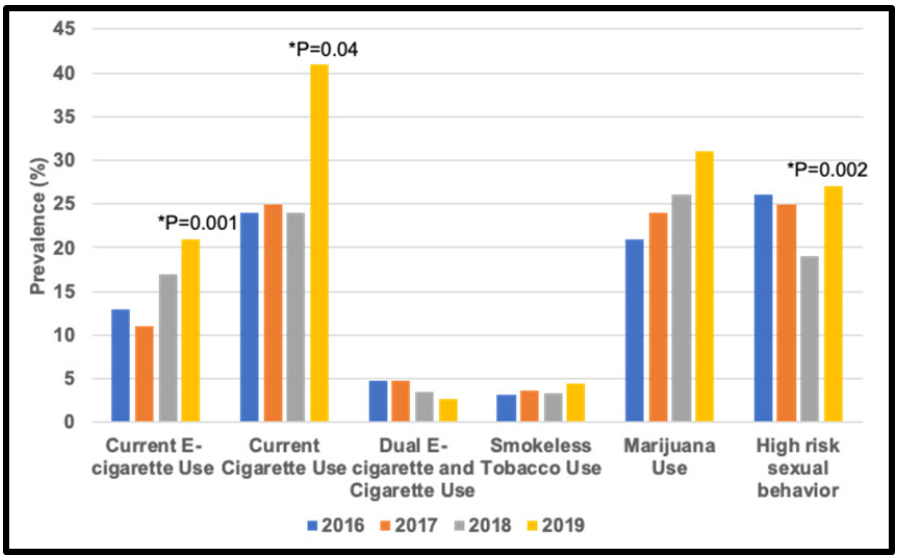

Figure 1. Trends in prevalence of risk behaviors among LGBT adults between the years 2016 and 2019.

DISCUSSION

In a nationally representative U.S. sample, the prevalence of current e-cigarette use among LGBT adults is 13%, almost twice that of heterosexual adults. LGBT adults are more likely to report current use of e-cigarettes, cigarettes, and marijuana, as well as high-risk behaviors compared to heterosexual adults. These results are similar in all age groups and among men and women who are LGBT. Finally, there is a time trend with increasing e-cigarette use and regular cigarette smoking over time.

A prior analysis from the 2016 BRFSS data showed that transgender as compared to cisgender adults were not more likely to smoke cigarettes currently and ever use e-cigarettes after adjusting for demographic factors.[11] Our study used more recent data from the 2017 and 2018 BRFSS datasets, therefore, had higher statistical power to study the association between LGBT and risk behaviors given the increasing prevalence of e-cigarettes over time in the U.S.[12] and the larger sample size of adults.

Another study showed that LGBT adults were twice as likely to report current e-cigarette use compared to heterosexual adults.[13] Consistent with these prior reports, LGBT adults were nearly twice more likely to use e-cigarettes compared to heterosexuals in our analysis of a nationally representative cohort of U.S. adults. The higher likelihood of e-cigarette use and other risk behaviors among LGBT adults may be in part due to burden of mental illness[14,15] resulting from stigmatization and discrimination from family or society. A prior study also has shown that sexual identity disorder is associated with both cigarette smoking and e-cigarette use among high school students.[16] Our study did not include adults younger than 18 years old, though subgroup analyses by age showed that our results were broadly consistent across different age groups.

Concerted efforts are required to educate the LGBT community about the potential harms of e-cigarette use given misconceptions about their safety. This misconception is likely the result of marketing strategies that promote e-cigarettes as safer alternatives to smoking.[17] Dual use of e-cigarettes and cigarettes was higher among LGBT compared to heterosexual adults. Our results also showed that there is a higher likelihood of such behaviors with e-cigarette use. LGBT adults may be at a higher risk of adverse cardiovascular health consequences from both traditional smoking and e-cigarette use. Clinicians treating LGBT adults may need to screen specifically for e-cigarettes, in addition to other associated risk behaviors, and educate them regarding potential harms.

Since our variables were all self-reported, they are subject to misclassification. Reasons underlying risk behaviors could not be evaluated. While we adjusted for multiple covariates in the analysis, there remained the possibility of residual confounding.

In conclusion, there are disparities in e-cigarette and other risk behaviors among LGBT adults, which may increase the risk of adverse health effects in this vulnerable population.

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Keywords: sexual and gender minorities, e-cigarettes, smoking, Behavioral Risk Factor Surveillance System

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Fibroadenoma Presenting as a Vulvar Mass

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Received Aug. 11, 2020; Accepted for publication Sept. 10, 2020; Published online Dec. 11, 2020
https://doi.org/10.17161/kjm.vol13.14549

INTRODUCTION

Ectopic breast tissue is very rare and found most commonly in the axilla; however, the vulva is the second most common location.[1] It is estimated that ectopic breast tissue occurs in 2% to 6% of women in the general population, with the vulva considered a rare site.[2] In 2012, there were 10 reported cases of ectopic breast tissue on vulva worldwide.[3] This tissue can arise anywhere along ectodermal primitive milk streaks as a result of incomplete involution during embryonic development.[4] While the cause of a new presenting vulvar mass may be unclear, a previous case report suggested that ectopic breast tissue in the vulva can be related to pregnancy, and should be suspected in a patient presenting with an enlarging mass in the postpartum period.[2] Other causes of breast tissue in the vulva are thought to be a normal part of the anogenital area, as these lesions can look very similar to mammary glands, but there is very limited literature as most masses have been reported as ectopic breast tissue.[5] Since ectopic breast tissue functions in the same way as normal breast tissue, the ectopic tissue is subject to hormonal stimulation, thus often appearing in pregnancy, with lactation, or with menstrual cycles.[2]

Imaging, such as magnetic resonance imaging, has been used in other cases for characterizing mass lesions,[1] however, in this case report, the mass originally was suspected to be a lipoma based on physical exam. To confirm the diagnosis, the tissue must be biopsied and assessed histologically.[2] While there are other case reports of breast tissue in the vulva, it is extremely rare with various presentations, so further discussion is warranted. Breast cancer and fibroadenomas also have been reported on the vulva, so benign and malignant neoplastic processes should be on the differential for masses discovered in the vulvar region.[1,6-9]

This report described a unique case of a unilateral vulvar mass found to be breast tissue. While vulvar masses associated with pregnancy and recurrence have been reported previously in the literature, this case was unique as the cause of this vulvar mass is unknown and completely random, with no associated conditions or correlation with pregnancy, lactation, or menstrual cycles or previous history of malignancy.[1,2,10,11]

CASE REPORT

A 44-year-old woman presented to the gynecology clinic after a mass that had been present for two years had become increasingly uncomfortable. The patient reported itchiness and she also had concerns that the mass was increasing in size. She denied any purulent discharge or erythema around the area. The patient had no significant medical or family history.

The patient presented to a family medicine clinic for evaluation of the mass. Due to its size, she was referred for evaluation by a gynecologist. On physical exam, a 2 x 3 cm rubbery, mobile, nontender mass was present on the external genitalia, 3 cm lateral to the clitoris and near the mons. The remainder of her genital exam was normal.

Due to the size of the mass and discomfort the patient was experiencing, the patient underwent an uncomplicated excisional biopsy completed under spinal anesthesia. A 2 cm incision was made on the inferior portion of the mass and it was resected away from normal skin with Metzenbaum scissors. This was continued until the base was reached. The right labial 2.4 x 2.4 x 1.1 cm pink-tan nodule was removed in whole and sent to pathology in formalin. The specimen was sectioned serially to reveal pink-tan fibrous cut surfaces. The final pathology report was consistent with benign fibroadenoma, and the surgical pathologist reported that there was no normal breast tissue, which implies that this is likely a fibroadenoma arising from anogenital mammary-like glands rather than arising from ectopic breast tissue (Figures 1 and 2). At her follow up visit two weeks post-surgery, the patient reported no concerns. Her biopsy site was healing well with no signs of infection. No other imaging or diagnostic assessments were performed.

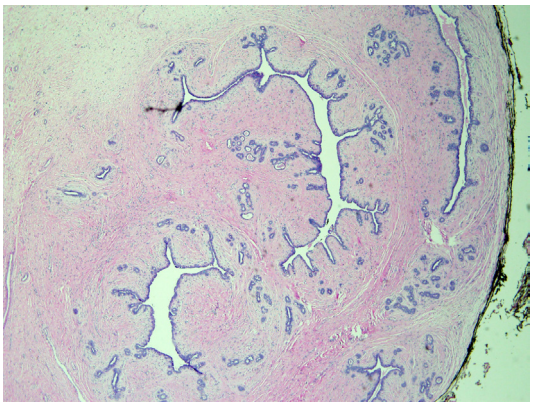

Figure 1. The biphasic lesion is composed of large, irregularly branching ducts and smaller glands in a lobular arrangement surrounded by hypocellular, dense collagenous stroma. The periphery of the lesion appears well-circumscribed but unencapsulated. (Image 4x)

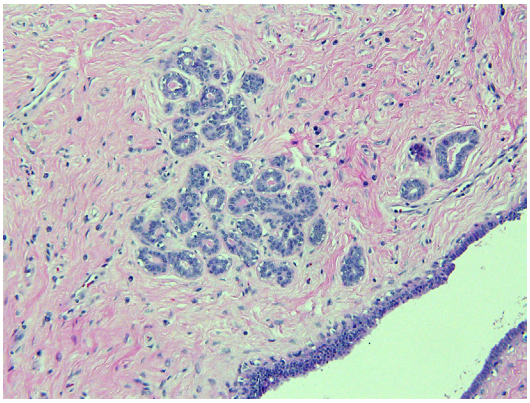

Figure 2. Both the stromal and epithelial components are cytologically bland and lack mitoses. Scattered myoepithelial cells with clear cytoplasm easily are identified surrounding the ducts and glands. The histologic appearance is identical to fibroadenoma of the breast. (Image 20x)

DISCUSSION

Ectopic breast tissue is a benign finding that can present as a vulvar mass. Clinicians providing routine gynecologic care may encounter this rare finding in the course of their career.

Ectopic tissue in women most frequently can be found in the axilla, but also anywhere along the milk line as well as beyond it.[4] The ectopic tissue can become tender with menstrual cycles and experience pathology, similar to what is expected of normally located breast tissue. Other cases of ectopic breast tissue in post-menopausal women have been reported, indicating that the glands can remain dormant for many years, then present after menopause has occured.[12]

Common pathologies that can be found in ectopic breast tissue include fibrocystic changes, mastitis, fibroadenoma, and carcinoma.[4,6-9] Specifically, pathologic cases of ectopic breast tissue with adenocarcinoma, intraductal papilloma, and fibroadenoma have been reported. Vulvar fibroadenomas initially may be misdiagnosed as an epidermal cyst, follicular cyst, Bartholin's gland-duct cyst, or lipoma and can be confirmed only with biopsy.[13]

Determining the type of ectopic breast tissue present is important because management will differ. There were cases of malignant ectopic breast tissue that were managed with immunohistochemical staining and sentinel lymph node biopsy, and hormone therapy.[14-18] Due to the rarity of these conditions, there are no clear guidelines on management. As in the case presented here, fibroadenomas can arise from anogenital mammary-like glands. Many causes of ectopic breast tissue have been reevaluated due to the recognition of mammary-like anogenital glands (MLAG), which are a normal constituent of the vulva.[19] Further evidence that this tissue is most likely due to MLAG, as opposed to ectopic breast tissue, is that vulvar MLAG cannot be derived from the mammary ridges or milk lines since the breast and vulva are separated widely by time and space.[19] Since MLAG tissue can contain features consistent with eccrine or apocrine tissue, these glands are most likely the cause of masses presenting in the anogenital region.

The diagnosis of breast tissue in the vulva can be done with fine needle aspiration cytology or excisional and incisional biopsy.[4] For symptomatic masses, the breast tissue should be excised completely to prevent recurrence of symptoms. In this case, the patient presented with an enlarging mass associated with pruritis with complete resolution of her symptoms after surgical removal. To our knowledge, there is no previous case report on a mass with pruritis as a presenting symptom. There is limited literature describing ectopic breast tissue in the vulva presenting as an enlarging mass over time.[2,10,13,20] One report specifically described vulvar ectopic breast tissue presenting as an abscess with pain and discharge, as well as vulvar swelling that had increased in size over the course of two years.[10]

In our case, the patient has not had any recurrence of symptoms to date; however, recurrent vulvar breast fibroadenoma has been reported in the literature and estimated to be around 3%.[3] Based on this report, masses that were greater than 2 cm or masses with incomplete removal were associated with higher risks of recurrence, so further surveillance and close follow-up is warranted for larger masses and those with concerning features. An asymptomatic nodule in the vulva consistent with fibroadenoma of the breast also has been reported.[13] Vulvar masses can present at any age with various symptoms, and both benign and malignant masses should be considered. It would be reasonable to include ectopic tissue, as well as mammary-like glands of the vulva, on the differential for vulvar pruritis when no other obvious pathology is identified, as pruritus can be a preceding sign of vulvar masses that are too small to be detected. A misdiagnosis of vulvar masses as ectopic breast tissue instead of mammary-like glands which are normal in the vulva should be considered in other cases.

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Keywords: breast, vulvar neoplasm, vulvar disease, fibroadenoma

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Generalized Rash and Bilateral Retinal Necrosis in an Adult Healthcare Worker after Post-Exposure Herpes Zoster Vaccination: A Rare Case Report

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Received June 26, 2020; Accepted for publication Sept. 22, 2020; Published online Dec. 11, 2020
https://doi.org/10.17161/kjm.vol13.13808

INTRODUCTION

Chickenpox is an acute and highly contagious infection caused by the varicella-zoster virus (VZV).[1] Varicella-zoster virus (VZV) is an exceptionally infectious virus. It presents as chickenpox when primary infection occurs and as herpes zoster (HZ) when it reactivates. The U.S. Centers for Disease Control and Prevention (CDC) recommend administering the VZV vaccine at baseline to every non-immune healthcare worker. In the event of exposure to VZV, CDC recommends immediate vaccination to prevent the dissemination of infection and furlough from the workplace for 10 - 21 days.[2]

Since 2006, the Advisory Committee on Immunization Practices (ACIP) recommends varicella vaccination (Varivax®) as a routine two-dose vaccine for children older than 12 months.[3] Zoster vaccine (Zostavax®) was approved by the U.S. Food and Drug Administration (FDA) to prevent shingles among adults 60 years and older, with or without the prior history of reported infection.[4] The FDA has expanded the vaccination administration for those who are 50 years and older. However, there were no studies present on the safety of this vaccine in those who had a history of zoster in the past. The implementation of universal immunization in children against varicella has led to a decrease in varicella incidence by 85%; however, about 30% of the adult population can still develop herpes zoster.[3]

In the healthcare settings, susceptible (non-immune) persons of all ages are at higher risk for severe varicella disease. Generalized rash from varicella vaccine is uncommon and described in 1 - 5% of the vaccinated persons, usually characterized by 5 - 50 lesions; however, it is enormously contagious. Herpes zoster involvement of the trigeminal nerve of the ophthalmic division can lead to distressing consequences. It is thought to be a result of cell-mediated immunity against the viral antigens in the eye.[5] There are two types of vaccines available in the U.S. Varivax®, a live attenuated varicella vaccine, has been reported to cause many ocular complications.[6] On the other hand, Zostavax® has been linked to fewer ocular complications. Despite that fact, a case of interstitial keratitis in a 50-year-old woman, 35 days after receiving the Zostavax® vaccine, has been reported.[7] She also had manifested multiple recurrences of her ocular disease expositions.

In this case report, a health worker case was described who developed generalized body rash and bilateral retinal necrosis 7 weeks and 14 weeks after the post-exposure vaccine, respectively.

CASE REPORT

A 42-year-old, male health worker was exposed to another health worker who had developed a typical chickenpox rash in a tertiary care hospital before being diagnosed. The patient was found non-immune, furloughed for days 10 - 21, and vaccinated with varicella vaccine three weeks after exposure. The patient's general past medical history was insignificant, with no varicella disease as a child. He also denied any immunodeficiency or other vaccine contraindications. The patient also had an unremarkable ophthalmological history in the past. However, at seven weeks after exposure (four weeks after vaccination), the patient presented at occupational health service (OHS) with generalized vesicular rash, characteristic for chickenpox. The health care worker also reported malaise, arthralgia, and body aches. The patient denied any fever. On physical examination, he had numerous widespread vesicles with erythematous bases all over the body. Molecular testing of a specimen from one of the rash lesions was positive for varicella-zoster virus (VZV). Subsequent analysis of markers that discriminate against the vaccine strain (Oka virus) from the wild type strain (open reading frame ORF 38 and ORF54) indicated that the patient VZV strain was consistent with the Oka virus vaccine and not wild type. Furthermore, vaccine strain-specific markers (ORF62) indicated that the patient VZV strain was consistent with the Oka virus vaccine. He was treated with oral acyclovir for 10 days. The OHS recommended further investigations and immune system evaluation in primary care settings.

At 14 weeks after exposure, the patient presented again with symptoms of blurred vision. Ophthalmologic examination showed bilateral retinal necrosis. The fundus examination of both eyes showed the progressive retinal opacification and outer retinal necrosis. The intraocular pressures in both eyes were within the normal range of 16 - 18 mm Hg. Intravitreal sample for polymerase chain reaction (PCR) was positive for VZV with the same vaccine strain that was detected previously from the rash lesion.

Furthermore, VZV was found in the cerebrospinal fluid as well. The immunologic evaluation identified the Human Immunodeficiency Virus (HIV) with CD4 counts of 98/ml and a viral load of 266,000 RNA copies/ml. The polymerase chain reaction (PCR) results for cytomegalovirus, herpes simplex, and Toxoplasma gondii were negative.

Therapy and Course. The patient was treated with intravitreal injections of gancyclovir and foscarnet. He also had received systemic treatment with intravenous acyclovir and foscarnet. Highly active antiretroviral therapy (HAART) was started based on laboratory findings of positive human immunodeficiency virus (HIV) test and CD4 count. After the start of HAART therapy and treatment, his visual acuity improved within three weeks. This case represented the health damage of the healthcare worker beyond the customary level of vaccination side effects and response, so it was subjected to a notification to the public health authorities.

DISCUSSION

Varicella-zoster infection can rise as a result of natural exposure to the wild-type virus, or through the vaccination that contains a live attenuated virus.[1] This virus remains dormant in the dorsal root ganglia and can become reactivated in the later stage of life. Herpes zoster infection, also known as shingles, typically manifests as a

maculopapular rash along one or two dermatomes and usually does not cross the midline. However, disseminated infection can spread randomly across multiple dermatomes and have the potential to involve many internal body organs, such as lungs, liver, and central nervous system. Immunocompromised people are at a higher risk of developing a disseminated infection.[8]

Given the history of disseminated body rash and bilateral retinal necrosis, it is suggested that our patient had disseminated zoster due to the reactivation of the herpes zoster virus as a result of a live attenuated vaccine. Moreover, the Oka strain analysis test confirmed the cause of generalized body rash and ocular symptoms. The patient met the diagnostic criteria for acute retinal necrosis. According to the American Uveitis Society, acute retinal necrosis is defined as greater than 1 foci of retinal necrosis along with other criteria, such as retinal arterial involvement with occlusive vasculopathy, the progression of symptoms in the absence of active antiviral therapy, and finally a prominent inflammatory reaction in anterior and vitreous chambers.[9] Immunocompetent patients also may develop this, but immunocompromised individuals are more prone to severe disease. Moreover, more cases of acute retinal necrosis due to herpes simplex 2 virus have been observed in young people. In contrast, cases due to herpes simplex 1 or herpes zoster occur in the elderly.[10]

Even though many hundreds of thousands of people get vaccinated, complications of the vaccine as a result of virus replication rarely have been highlighted and reported.[11] A clinical trial study involving more than 60,000 individuals reported a possible but unconfirmed case of Oka strain rash development within six weeks of immunization.[11,12] Moreover, a case of Oka strain herpes zoster also has been reported after shingles vaccine administration, but there was no retinal involvement.[13] Heath et al.[14] reported a case of acute retinal necrosis caused by a zoster vaccine in an older patient with a confirmed Oka strain virus of the vaccine. There are two other cases of acute retinal necrosis after herpes zoster vaccination reported in the elderly, explaining the possible reactivation or infection by the Oka vaccine strain.[15] However, to our knowledge, there was no case reported with a combination of clinical presentation of generalized body rash and acute bilateral retinal necrosis due to the Oka HZ vaccine virus strain.

Intravenous acyclovir has been regarded as a standard treatment for acute retinal necrosis. However, current guidelines recommended using oral valaciclovir or valganciclovir to treat acute retinal necrosis due to herpes simplex/zoster and cytomegalovirus, respectively.[16] For those patients with valaciclovir resistance or with severe disease involving the optic nerve, intravitreal injection of foscarnet is recommended twice or thrice weekly. Oral corticosteroids are affected by patients with severe inflammation or sight-threatening disease with optic nerve involvement.[16]

In this case report, the patient was immunocompromised due to HIV and exhibited varicella-zoster infection seven weeks after the vaccination. His immune status put him at risk of disseminated varicella infection and acute retinal necrosis as it is one of the contraindications to the live attenuated vaccine.[17] Additionally, despite the standard intravenous antiviral therapy for disseminated viral infection, the patient developed acute retinal necrosis several weeks after vaccination.

CONCLUSIONS

In summary, a case of disseminated varicella infection and acute retinal necrosis was reported following varicella-zoster vaccination as a post-exposure protocol. This case highlighted that immunocompromised persons are at high risk for disseminated rash and disseminated VZV disease following vaccination. Immune deficiency should be sought in atypical vaccine reaction, even in the setting of healthcare worker exposure investigation.

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Keywords: varicella zoster virus infection, herpes zoster, acute retinal necrosis, skin rash, chickenpox vaccine

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VOLUME 13 • 2020

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