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Comparison of Hand Eczema Search Terms in Iraq Before and During SARS-CoV-2 Pandemic Using Frequentist Statistics and Polynomial Models

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ABSTRACT

Introduction. SARS-CoV-2 pandemic spread around the world exponentially. People use disinfectants excessively as a form of protection from the novel coronavirus, which may result in contact eczema. This, in turn, may be monitored by the local health authorities. Our study explores the internet in order to detect significant changes in online information search behaviors associated with eczema in Iraq during the pandemic.

Material and Methods. We searched the internet, via Google Trends, using five search terms; "اكزيما", "الاكزيما", "اكزيما اليد", "كحول", and "مطهر"; these are the Arabic translation for "eczema", "the eczema", "hand eczema", "alcohol", and "disinfectant". We explored the temporal mapping covering two years, before and during the pandemic, using frequentist statistics, polynomial models, and neural networks to evaluate the time series which reflects web users' information-seeking behavior with regard to these terms.

Results. Spatial mapping conveyed data from six Iraq governorates, including Ninawa, Babil, Al-Najaf, Baghdad, Basrah, and Erbil. Basrah governorate had the highest score (interest) for the search term "the eczema" (الاكزيما), while Al-Najaf had the highest score regarding the search term "disinfectant" (مطهر). Tempo-

ral mapping exhibited high variability, the highest of which was for the "the eczema" (الاكزيما) and "alcohol" (كحول). Exploring the time series using polynomial models demonstrated a weak power over the two years. However, in the course of the pandemic year, all models possessed moderate power.
Conclusions. Changes in the human behavior during pandemic events are of prime importance for the pharmacovigilance experts. Pandemics may affect medical conditions, including hand eczema, as a manifestation of disinfectants overuse. Combining statistics and artificial intelligence facilitates screening, detecting, and collecting pharmacovigilance safety data.

Introduction

Pharmacovigilance comprises the science and activities of detecting, assessing, understanding, and preventing adverse effects of drugs or drug-related problems [1]. Since its global expansion in the 1960s, following the thalidomide tragedy and for many drug safety interventions, such as drug withdrawals, labeling changes, and prescription restrictions, the aforementioned branch of science shows an exponential progression and importance in health programs. This, in turn, has led, over the last decade, to a fast evolution of regulation with more requirements from health authorities [2, 3]. In fact, the advancement of the internet, social media, and digital health data contributed to an additional increase of safety and effectiveness data, and have been accelerated by the current global pandemic due to the novel coronavirus 2019 (2019-nCoV). Additionally, the collection, detection, and assessment of the increasing safety data can be facilitated using artificial intelligence.

Since the initial reports of the Wuhan outbreak, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic has been spreading around the world at an alarmingly exponential rate [4, 5]. As of 25 February 2022, the confirmed infections exceeded 432,505,813 worldwide and 2,299,767 in Iraq [4]. Complications related to the illness claimed the lives of over 5,950,376 globally and 24,948 in Iraq [4.] Furthermore, SARS-CoV-2 affected nations from developed and developing countries; the most affected to date in total (cumulative) cases included the United States, India, Brazil, France, United Kingdom, Russia, Germany, Turkey, Italy, and Spain [4]. As a top priority for the global health agenda, scientists successfully developed several effective vaccines, including Pfizer–BioNTech (BNT162b2), Moderna (mRNA-1273), and AstraZeneca (AZD1222) [6-8]. However, novel mutant strains of the coronavirus disease 2019 (COVID-19) emerged, including those discovered in the United Kingdom (α variant), the delta variant (δ) in India, and the most recent omicron (O) variant in South Africa [9]. Until the vaccination campaign is extended to the entire world population and novel variants of the virus stopped to emerge – which is unlikely – the first preventive measures, such as social distancing, personal protective equipment, and hand disinfection must be maintained. In fact, new variants may persistently emerge and evade vaccine-induced immunity and the proclaimed natural "herd immunity".

People worldwide have been using disinfectants, including alcohol, as a form of protection from the novel coronavirus. Eczema (dermatitis), specifically contact eczema of the hand, are dermatological conditions that can manifest due to the overzealous use of those chemicals; nonetheless, Minamoto et al. (2016) carefully cited that chemical additives – such as sodium laureth sulfate (SLES) – may account for inducing an eczematous skin reaction, rather than alcohol itself [10]. Eczema may manifest as an acute or chronic condition, which mandates medical treatment to prevent subsequent complications, including those affecting the manual skills, which in turn may drastically impair the quality of life, particularly in the elderly [11]. We refer to everyday activities where we use our hands to manipulate physical objects, write, draw, and many other functions. The hand represents the prehensile, or grasping "organ", of human beings and primates. Therefore, the conditions affecting the musculoskeletal or motor anatomical units of the hand, its skin, or the haptic sensory feedback mechanisms may handicap, or reduce the functional capacity of the hand and its derived manual skills.

Our study aims to explore the internet by searching for adverse events (AE) terms related

to eczema, dermatitis, and disinfectants, in order to investigate the specific spatial-temporal patterns before and during the pandemic. Our primary objective is to detect significant changes in web search queries connected with eczema in Iraq that may relate to the overzealous use of disinfectants during the pandemic. We believe that the current study is essential for health officials at the Iraqi Ministry of Health and local pharmacovigilance authority. Using frequentist inference and artificial intelligence methods, our study may provide novel insights on the importance of the digital knowledge and safety data available via the world wide web to predict future trends during the pandemic, parallel phenomena, as well as safety surveillance of the pharmaceutical products [12-15].

Materials and Methods

We searched the internet, via Google Trends, using five search terms: "اكزيما", "الاكزيما", "اكزيما اليد", "كحول", and "مطهر" [16]. These terms are the Arabic language translation for "eczema", "the eczema", "hand eczema", "alcohol", and "disinfectant". We explored the web in the span of two years, one year before and one year during the pandemic, from 17th November 2018 to 17th November 2020, in order to compare the pre-pandemic versus the pandemic year (era) in connection with our study objectives. The date 17th November 2019 marks the emergence of SARS-CoV-2 in Wuhan in China [4, 5]. The authors know that the term "alcohol" is not limited to alcohol used for medicinal purposes and disinfection, and thus can also refer to alcoholic drinks and beverages. However, from the cultural standpoint, Iraqis do not refer to the latter category as "alcohol". Instead, they would rather refer to brand names, commercial, and public names from their native language.

We deployed the Shapiro-Wilk test to evaluate the normality distribution. Spearman's rank-order correlation was used to test potential significant correlations among search terms (web queries). The independent samples Mann-Whitney U test (nonparametric testing) compared the pre-pandemic versus the pandemic year. Polynomial modeling for each search term was conveyed to anticipate if the model properly fits the time series, representing web users' online information search behavior concerning the five terms of interest. A calculated probability of less than 0.05 (p-value < 0.05) was considered the cut-off margin for statistical significance. We processed the raw data with Microsoft Excel 2016 with Analysis ToolPak add-in, and we conducted data analytics and machine learning with IBM Statistical Package for the Social Sciences (SPSS) version 26.

We implemented the supervised machine learning using multilayer perceptron (MLP) neural networks based on the scaled conjugate gradient optimization algorithm and a default SPSS allocation of the training set and testing set at 70% and 30%, respectively. The MLP procedure uses a feedforward architecture – data only moves from input nodes through the hidden layer of nodes to output nodes – to produce a model for dependent (outcome) variables based on the values of one or more independent variables (predictors). The feedforward neural network represents a prototypical form of artificial neural networks (ANN). MLP generates synaptic weights and independent variables importance analysis. As opposed to the descendant and recurrent neural networks, in feedforward ANN connections between the nodes do not form a cycle.

Concerning the raw data, there were enough data points for each variable to train the neural network without overfitting. When considering the holistic period, there were 105 entries (data points) and 52 versus 53 data points for the pre-pandemic versus the pandemic period. Nonetheless, overfitting may also occur, as we consider the case of Iraq, not an aggregate of countries. The temporal resolution was one week at a time (weekly intervals); exploring Google Trends on a year-by-year basis provided the weekly-based temporal intervals.

The research did not mandate ethical approval, since we worked on open data publicly available on the internet via the Google Trends engine, and the study involves no patients.

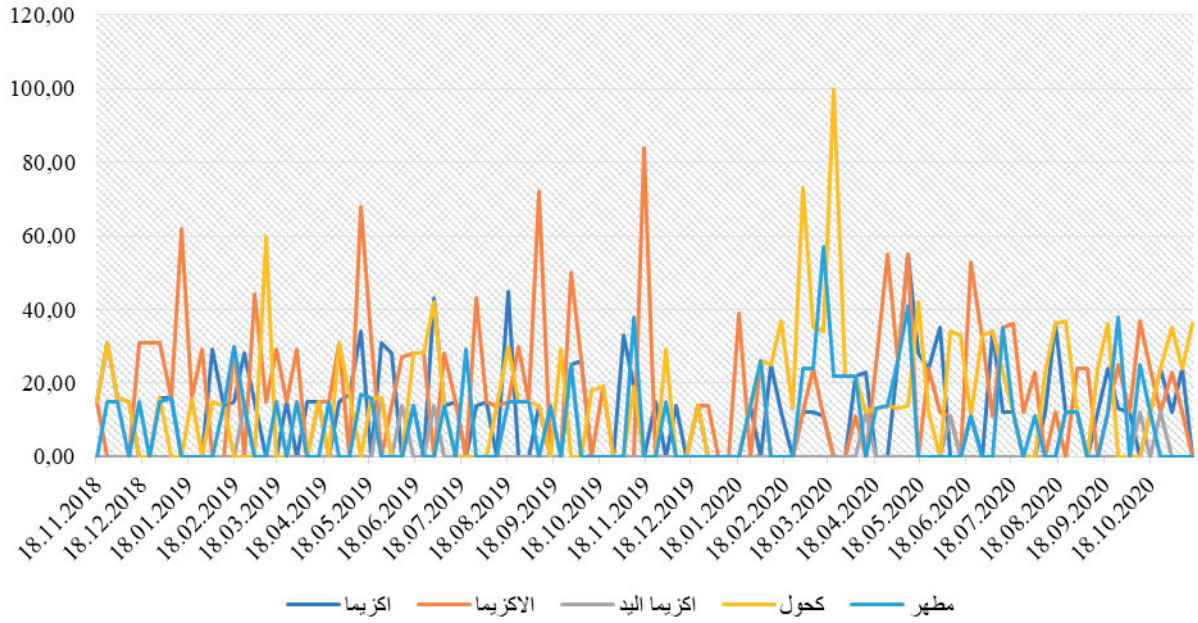
Results

Geographic (spatial) mapping, based on the analysis of the raw data retrieved from Google Trends website revealed forty countries with interest in the topic of the AE term "eczema" (اكزيما), the top

twenty of which included France, Malaysia, Singapore, Pakistan, Switzerland, Nigeria, Italy, Vietnam, Brazil, Saudi Arabia, New Zealand, United Kingdom, Kenya, Canada, Philippines, Hong Kong, Bangladesh, Australia, United Arab Emirates, and Ireland. Only three countries from the Arab world contributed to the spatial map, involving Saudi Arabia, United Arab Emirates, and Egypt. The top ten countries of highest interest in disinfectants comprised Brazil, Japan, Indonesia, Italy, Saudi Arabia, Egypt, Germany, Bangladesh, Switzerland, and Hong Kong. Iraq's spatial mapping conveyed data from six governorates, including Ninawa, Babil, Al-Najaf, Baghdad, Basrah, and Erbil. In contrast, data connected with the search term "اكزيما اليد" (hand eczema) were completely absent due to the inherent limitations of Google Trends itself. Basrah governorate had the highest score (interest) for the search term "الاكزيما" (the eczema), while Al-Najaf had the highest score for the search term "مطهر" (disinfectant).

On the other hand, temporal mapping (Figure 1) exhibited high variability, the highest of which was for the search terms "الاكزيما" (the eczema) (mean = 17.67 +/- standard error of mean = 1.773) and "كحول" (alcohol) (15.58 +/- 1.655), while the lowest of which was for the search terms "اكزيما" (eczema) (12.12 +/- 1.211), "مطهر" (disinfectant) (8.49 +/- 1.141), and "اكزيما اليد" (hand eczema) (1.47 +/- 0.437). We deployed polynomial modeling to explore the temporal variabilities within the time series for each search term (**Table 1**); we interpreted the strength of the correlation between time (x-axis, predictor variable), as well as the online information search behavior (y-axis, dependent variable) per the correlation coefficient. For the holistic period (two years), all models had a weak power with an exception for the model describing the temporal mapping of the search term "كحول" (alcohol) (R^2 score = 0.164; Correlation Coefficient = 0.406). Similarly, during the pre-pandemic year, all search terms presented models of weak power except for the search term "الاكزيما" (the eczema) (R^2 score = 0.109; Correlation Coefficient = 0.330). However, during the pandemic year, the models for each search term showed a moderate power (**Table 1**).

Using the Shapiro-Wilk test, none of the search terms had a normal distribution (p-value < 0.001), and the statistical outliers existed during February 2019, May and June 2019, August and September 2019, November 2019, February to June 2020, and August to October 2020. The highest number of statistical outliers was for the search term "اكزيما اليد" (hand eczema), and these were mainly clustered in the pandemic during April



* x = time, y = interest over the surface web.
** Pre-Pandemic (17th November 2018 to 17th November 2019), and pandemic (17th November 2019 to 17th November 2020).

Figure 1. Temporal Mapping of the Online Information Search Behaviour

Table 1. Polynomial Models

Era	Parameter	Order of Polynomial Function	R^2 Score	Correlation Coefficient	Correlation Coefficient Strength
Pre-Pandemic & Pandemic	كحول (alcohol)	6^{th}	0.164	0.406	Moderate
	اكزيما (eczema)	6^{th}	0.058	0.241	Weak
	اكزيما اليد (hand eczema)	6^{th}	0.049	0.221	Weak
	(disinfectant)	6^{th}	0.040	0.199	Weak
	الاكزيما (the eczema)	6^{th}	0.039	0.198	Weak
Pre-Pandemic	الاكزيما (the eczema)	6^{th}	0.109	0.330	Moderate
	اكزيما (eczema)	6^{th}	0.072	0.296	Weak
	مطهر (disinfectant)	6^{th}	0.080	0.283	Weak
	كحول (alcohol)	6^{th}	0.056	0.236	Weak
	اكزيما اليد (hand eczema)	6^{th}	0.052	0.229	Weak
Pandemic	كحول (alcohol)	6^{th}	0.258	0.508	Moderate
	مطهر (disinfectant)	6^{th}	0.234	0.484	Moderate
	الاكزيما (the eczema)	6^{th}	0.176	0.420	Moderate
	اكزيما (eczema)	6^{th}	0.1405	0.375	Moderate
	اكزيما اليد (hand eczema)	6^{th}	0.123	0.351	Moderate

* x = time, y = interest over the surface web.
** Pre-Pandemic (17^{th} November 2018 to 17^{th} November 2019), and pandemic (17^{th} November 2019 to 17^{th} November 2020).

2020, June 2020, August 2020, and October 2020. For the holistic period, bivariate correlations confirmed the existence of a statistically significant correlation for "الاكزيما" (the eczema) versus "مطهر" (disinfectant) (Spearman's rho Correlation Coeffecient = 0.221, p-value = 0.024) and "اكزيما" (the eczema) versus "كحول" (alcohol) (-0.268, 0.006). Nonetheless, each of these two correlations had a weak effect size. During the pre-pandemic period, there was only one significant correlation, although also of weak effect size, for the search term "اكزيما" (eczema) versus "اكزيما اليد" (hand eczema) (Spearman's rho Correlation Coeffecient = 0.291, p-value = 0.037). For the pandemic period, there was a statistically significant correlation for "الاكزيما" (the eczema) versus "مطهر" (disinfectant) (Spearman's rho Correlation Coeffecient = 0.359, p-value = 0.008) and "الاكزيما" (the eczema) versus "كحول" (alcohol) (-0.271, 0.049), of moderate and weak effect size, respectively (**Table 2**). Furthermore, nonparametric testing via the Mann-Whitney U test for the pre-pandemic versus the pandemic year detected a significant difference for one search term only, "كحول" (alcohol), which is in favor of the pandemic year (p-value = 0.036) (**Table 3** and **Figure 2**).

Considering the previous statistical inference and the existing evidence within the dermatology literature [17, 18], it is plausible that a causal relationship exists; the pandemic event might have affected web users with regard to searching for those five specific search terms. We are assuming that web queries using the two search terms "كحول" (alcohol) and "مطهر" (disinfectant), represent or reflect the independent variables (predictors). In comparison, the remain-

ing three terms that are related to AE terms concerning eczema and hand eczema represent the dependent variables (outcomes). Accordingly, we conducted a supervised machine learning model (**Table 4**), via neural networks for the holistic period, for which, the predictors' importance analysis conveyed higher importance for "كحول" (alcohol) (importance = 0.569, normalized

Table 2. Nonparametric Bivariate Correlations: Pandemic Era

		اكزيما (eczema)	الاكزيما (the eczema)	اكزيما اليد (hand eczema)	كحول (alcohol)	مطهر (disinfectant)
اكزيما (eczema)	Correlation Coefficient	1.000	-.046	.030	.198	-.016
	Sig. (2-tailed)	.	.744	.831	.155	.907
	N	53	53	53	53	53
الاكزيما (the eczema)	Correlation Coefficient	-.046	1.000	-.026	-.271*	.359**
	Sig. (2-tailed)	.744	.	.853	.049	.008
	N	53	53	53	53	53
اكزيما اليد (hand eczema)	Correlation Coefficient	.030	-.026	1.000	.031	.012
	Sig. (2-tailed)	.831	.853	.	.823	.931
	N	53	53	53	53	53
كحول (alcohol)	Correlation Coefficient	.198	-.271*	.031	1.000	.162
	Sig. (2-tailed)	.155	.049	.823	.	.245
	N	53	53	53	53	53
مطهر (disinfectant)	Correlation Coefficient	-.016	.359**	.012	.162	1.000
	Sig. (2-tailed)	.907	.008	.931	.245	.
	N	53	53	53	53	53

* Correlation is significant at the 0.05 level (2-tailed).
** Correlation is significant at the 0.01 level (2-tailed).

Table 3. Hypothesis Test Summary: Pre-Pandemic vs. Pandemic

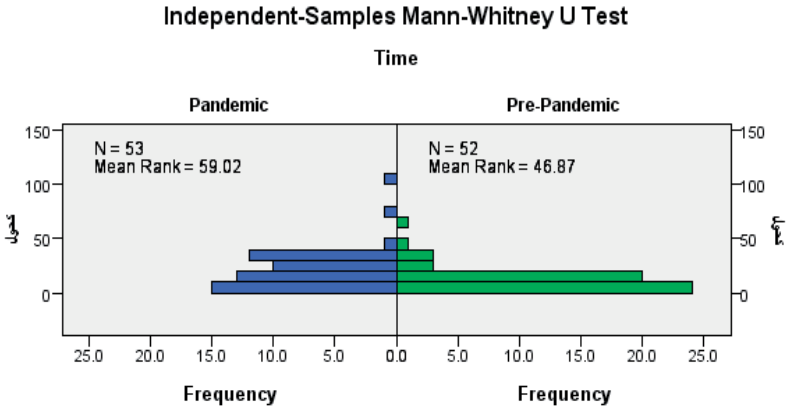
Hypothesis Test Summary

	Null Hypothesis	Test	Sig.	Decision
1	The distribution of اكزيما is the same across categories of Time.	Independent-Samples Mann-Whitney U Test	.272	Retain the null hypothesis.
2	The distribution of الاكزيما is the same across categories of Time.	Independent-Samples Mann-Whitney U Test	.177	Retain the null hypothesis.
3	The distribution of اكزيما اليد is the same across categories of Time.	Independent-Samples Mann-Whitney U Test	.918	Retain the null hypothesis.
4	The distribution of كحول is the same across categories of Time.	Independent-Samples Mann-Whitney U Test	.036	Reject the null hypothesis.
5	The distribution of مطهر is the same across categories of Time.	Independent-Samples Mann-Whitney U Test	.943	Retain the null hypothesis.

Asymptotic significances are displayed. The significance level is .05.

* Pre-Pandemic: 17th November 2018 to 17th November 2019 and Pandemic: 17th November 2019 to 17th November 2020
** اكزيما (eczema), الاكزيما (the eczema), اكزيما اليد (hand eczema), كحول (alcohol), مطهر (disinfectant)

importance = 100.0%) than "مطهر" (disinfectant) (0.431, 75.7%). In terms of the pre-pandemic year, the neural networks validated somewhat similar results for "كحول" (alcohol) (importance = 0.523, normalized importance = 100.0%) and "مطهر" (disinfectant) (0.477, 91%). As for the pandemic year, the independent variables' importance also assigned a weight that is higher for "كحول"



Total N	105
Mann-Whitney U	1,059.000
Wilcoxon W	2,437.000
Test Statistic	1,059.000
Standard Error	151.894
Standardized Test Statistic	-2.100
Asymptotic Sig. (2-sided test)	.036

* Pre-Pandemic: 17th November 2018 to 17th November 2019

** Pandemic: 17th November 2019 to 17th November 2020

Figure 2. Hypothesis Testing: Pre-Pandemic vs. Pandemic for Search Term "كحول" (alcohol)

Table 4. Supervised Machine Learning: Model Summary

Training	Sum of Squares Error		106.648
	Average Overall Relative Error		1.001
	Relative Error for Scale Dependents	اكزيما (eczema)	.994
		الاكزيما (the eczema)	.993
		اكزيما اليد (hand eczema)	1.017
	Stopping Rule Used		One consecutive step(s) with no decrease in error [a]
	Training Time		0:00:00.03
Testing	Sum of Squares Error		47.896
	Average Overall Relative Error		.981
	Relative Error for Scale Dependents	اكزيما (eczema)	.969
		الاكزيما (the eczema)	1.004
		اكزيما اليد (hand eczema)	.947

a – Error computations are based on the testing sample

(alcohol) (importance = 0.547, normalized importance = 100.0%) compared to "مطهر" (disinfectant) (0.453, 82.9%).

Discussion

The temporal mapping provided much data concerning our study objectives. Furthermore, we could map the temporal variations connected with the search terms with a higher temporal resolution, using polynomial models, during the pandemic. Bivariate correlations existed before and during the pandemic; however, the correlations were radically different. Contrary to our pre-study anticipation, AE search terms related to eczema and hand eczema did not significantly differ before and during the pandemic. Nevertheless, the web users searched significantly more for the term "كحول" (alcohol) during the pandemic. Thus, these results may indicate a significant increase in alcohol use for disinfection, although not a significant increase in eczema and hand eczema cases in Iraq during the pandemic. ANN analytics verified potential causality between the terms related to disinfectants as well as those related to the AE terms of eczema.

Statistical analyses for the pandemic period confirmed that there was a statistically significant correlation for "الاكزيما" (the eczema) versus "مطهر" (disinfectant) (Spearman's rho Correlation Coeffecient = 0.359, p-value = 0.008). Additionally, a significant increase was observed in the search volume for alcohol during the pandemic compared to the pre-pandemic. Furthermore, each of the polynomial models became stronger (moderate strength) when compared to the pre-pandemic, in which most of the models (4/5, 80%) had a weak strength (**Table 1**). Accordingly, the COVID-19 pandemic might have induced a change in human behavior, including online information search behavior reflected as the web search volume on the Google Trends website. Our study does not provide much concerning positive findings; besides, the calculated effect size was weak most of the time. Nonetheless, the effect size can vary from one country to another, bearing in mind the population size and other demographic parameters. Our research represents a piece of supporting evidence which may complement and guide future studies worldwide.

Machine learning is a subfield of computer science which learns patterns from data without providing explicit programming instructions to create algorithms intended to perform a specific task [12]. As a modality of narrow artificial intelligence (nAI), machine learning represents a powerful tool for researchers which can substantially reduce the considerable burden on the healthcare system and the economy during the pandemic [19]. Non-clinical research methods, such as machine learning, data mining, deep learning, and other nAI modalities may also facilitate the diagnosis and prognosis for SARS-CoV-2 pandemic patients. Few other studies discussed the condition of hand eczema during the COVID-19 pandemic, including Singh et al. (2020) and Bilcharz et al. (2020). In fact,they demonstarted that overzealous use of sanitizers and frequent hand washing might cause hand eczema due to a disrupted skin barrier. Additionally,they also reported an increasein the incidence of new-onset hand eczema within the general population due to the overzealous hand hygiene [17, 18]. In parallel with the previously mentioned studies, we emphasize the integration of ML and nAI with classical (frequentist) statistics for studying the digital epidemiology and the spatio-temporal analysis of the pandemic and collateral phenomena [20–24].

The rationale for implementing machine learning relies on five elements: (1) Collateral – supporting – evidence based on machine learning algorithms. (2) An alternative method to classical data analytics. (3) Reconciliation of frequentist inference with neural networks models. (4) A form of convergent thinking, dealing with digital epidemiological research questions from alternative perspectives. (5) A supporting method for future research in pharmacovigilance, pharmacotherapy, dermatological sciences, and digital epidemiology.

One of the study limitations is that the pandemic could have limited access to the healthcare institutions to some extent, and this would consequently result in the need to search for alternative solutions to health problems and diseases via the internet. Nonetheless, in Iraq, the healthcare system – as in all developing countries – is different and much inferior to that of the developed world, including Poland and the European Union. Another limitation was the inability to differentiate whether the search for alcohol was related

to medicinal alcohol, or to alcoholic beverages; hence, some false-positive results are possible. However, we believe that alcoholic drinkers in Iraq might search for alternate terms, such as "بيرة" (beer) and "عرك" (gin), rather than the term "كحول" (alcohol) per se. Moreover, another limitation is the absence of Arabic combined terminology for the search term "اكزيما اليد" (hand eczema), which also reflects the built-in limitations of the Google Trends website itself. We are aware that our study may only be considered as the supporting (collateral) evidence due to the nature of the study design, intrinsic (inherent) limitations of the Google Trends website, and the potentially non-specific mapping terms used to explore the spatiotemporal mapping of data from Google Trends. Therefore, subsequent robust pre-clinical and clinical research is mandatory to confirm our hypotheses and observations. Additionally, Google Trends also possesses inherent limitations and restrictions; for instance, the search results available through Google Trends are anonymous and only reflect individuals with internet access, potentially excluding specific groups of interest, for example, the elderly, terminally ill patients, the disabled, and underprivileged groups who lack access to the internet in low- and middle-income countries [25]. Furthermore, Google Trends only conveys relative numbers – a relative interest at a percentile scale – and there is no official way yet to access real absolute numbers. Google Trends also derive data from web users utilizing Google search engine only; therefore, web queries based on other search engines, including DuckDuckGo, Ecosia, Dogpile, WolframAlpha, Gigablast, Startpage, and Qwant, will not be mapped.

Our research has other limitations inherent to the observational study design, including a lower level of evidence than the experimental or quasi-experimental studies, hence it is prone to biases and confounding variables, and the reduced capacity to infer causality. Additionally, web users may avoid being tracked while surfing the web. Internet users can rely on internet protocol (IP) masking, virtual private networks (VPN), VPN applications, or utilizing web browsers and engines dedicated to anonymous internet use, including Tor browser and DuckDuckGo search engine [26]. Furthermore, web users in certain countries, such as the People's Republic of China (PRC), are obliged to use alternative national search engines due to the governmental policies and regulations; for instance, Baidu is the dominant internet search engine company in the PRC [27].

The findings can be summarized into 1) COVID-19 pandemic has impacted the manner in which disinfectants are used, which might result in adverse events, such as eczema and dermatitis due to disinfectants overuse, or because of chemical additives in alcohol. 2) Due to the pandemic, online information-seeking behavior has become more evident and manifested as Google Trends' search volume, which is one way to understand the magnitude of the problem. 3) Using artificial intelligence may facilitate the screening, detecting, and collecting safety data, extending to other health products.

During the pandemic, changes in human behavior, including online information search behavior, are of prime importance, not only to sociologists and psychologists, but also to physicians, epidemiologists, and pharmacovigilance specialists. Therefore, four key messages can be highlighted: 1) Pandemics, as rare events, might affect medical conditions which indirectly relate to the event itself, as in the case of hand eczema as a manifestation of disinfectants overuse. 2) Dermatologists can collaborate with data scientists to realize the applicability of big data for evidence-based pharmacovigilance. 3) Digital data are worthy of exploration from epidemiological and pharmacovigilance perspectives to guide the subsequent research of the higher level-of-evidence hierarchy, including randomized controlled trials and meta-analytic studies. 4) Our research methodology and results can be regarded as supporting evidence for the subsequent aggregate studies worldwide.

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Conflict of interest statement
The authors declare that there are no competing interests. The authors have self-funded the study; no external funding exists. The authors have no competing interests. Dr. Ahmed Al-Imam is a participant in the STER Internationalisation of Doctoral Schools Programme from NAWA Polish National Agency for Academic Exchange No. PPI/STE/2020/1/00014/DEC/02.

Availability of Data
Our data are available upon request from the corresponding author and within three years from the article's publication date.

Contribution of Authors
Ahmed Al-Imam (AA) collected the raw data, conceptualized the research and statistical hypotheses, conducted data analytics, and wrote the article's first draft. Nada Al-Ward (NAW), Manal M Younus (MMY), Omar Aimer (OA), and Ali K Al-Shalchy (AKA) contributed to revising the first draft, developing the discussion section, and enhancing its scholarly quality.

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References

1. Safety monitoring of medicinal products. Guidelines for setting up and running a pharmacovigilance center. Uppsala, WHO Collaborating Centre for International Drug Monitoring, 2000.
2. Alomar M, Palaian S, Al-Tabakha MM. Pharmacovigilance in perspective: drug withdrawals, data mining and policy implications. F1000Res. 2019; 8: 2109.
3. Foppiano M, Lombardo G. Worldwide pharmacovigilance systems and tolrestat withdrawal. The Lancet. 1997; 349(9049): 399–400.
4. Worldometer - real time world statistics [Internet]. Worldometer. 2020 [cited 22 January 2021]. Available from: https://www.worldometers.info/
5. Motyka MA, Al-Imam A, Aljarshawi MHA. SARS-CoV-2 pandemic as an anomie. Przestrzeń Społeczna (Social Space). 2;2020 (20): 111–144.
6. Wadman M. Public needs to prep for vaccine side effects. Science. 2020; 370(6520): 1022.
7. Logunov DY, Dolzhikova IV, Shcheblyakov DV, Tukhvatulin AI, Zubkova OV, Dzharullaeva AS, Kovyrshina AV, Lubenets NL, Grousova DM, Erokhova AS, Botikov AG. Safety and efficacy of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine: an interim analysis of a randomised controlled phase 3 trial in Russia. The Lancet. 2021; 397(10275): 671–81.
8. COVID-19 vaccine tracker [Internet]. The Regulatory Affairs Professionals Society (RAPS). 2020 [cited 22 April 2021]. Available from: https://www.raps.org/news-and-articles/news-articles/2020/3/covid-19-vaccine-tracker
9. Papanikolaou V, Chrysovergis A, Ragos V, Tsiambas E, Katsinis S, Manoli A, Papouliakos S, Roukas D, Mastronikolis S, Peschos D, Batistatou A. From Delta to Omicron: S1-RBD/S2 mutation/deletion equilibrium in SARS-CoV-2 defined variants. Gene. 2022; 814: 146134.
10. Minamoto K, Watanabe T, Diepgen TL. Self-reported hand eczema among dental workers in Japan - a cross-sectional study. Contact Derm. 2016; 75(4): 230–239.
11. Agner T, Andersen KE, Brandao FM, Bruynzeel DP, Bruze M, Frosch P, et al. Hand eczema severity and quality of life: a cross sectional, multicentre study of hand eczema patients. Contact Derm. 2008; 59(1): 43–7.
12. Al-Imam A, Abdul-Wahaab IT, Konuri VK, Sahai A. Reconciling artificial intelligence and non-Bayesian models for pterygomaxillary morphometrics. Folia Morphol. 2021; 80(3): 625–641.
13. Al-Imam A, Motyka MA, Jędrzejko MZ. Conflicting Opinions in Connection with Digital Superintelligence. IAES Int J Artif Intell. 2020; 9(2): 336–348.
14. Al-Imam A, Al-Lami F. Machine Learning for Potent Dermatology Research and Practice. J Dermatol Dermatol Surg. 2020; 24(1): 1–4.
15. Al-Imam, A. Inferential Analysis of Big Data in Real-Time: One Giant Leap for Spatiotemporal Digital Epidemiology in Dentistry. Oral Implantol. 2019; 12(1): 1–14.
16. Google Trends. 2020 [cited 22 January 2021]. Available from: https://trends.google.com/
17. Singh M, Pawar M, Bothra A, Choudhary N. Overzealous hand hygiene during the COVID 19 pandemic causing an increased incidence of hand eczema among general population. J Am Acad Dermatol. 2020; 83(1): e37-e41.
18. Blicharz L, Czuwara J, Samochocki Z, et al. Hand eczema-A growing dermatological concern during the COVID-19 pandemic and possible treatments. Dermatol Ther. 2020; 33(5): e13545.
19. Abatemarco D, Perera S, Bao SH, Desai S, Assuncao B, Tetarenko N, Danysz K, Mockute R, Widdowson M, Fornarotto N, Beauchamp S. Training augmented intelligent capabilities for pharmacovigilance: applying deep-learning approaches to individual case safety report processing. Pharm Med. 2018; 32(6):391–401.
20. Al-Imam A, Gorial FI, Al-shalchy A. A Novel Unusual Manifestation of CH-Alpha as Acute Metabolic Disturbances: Case Report and Big Data Analytics. J Fac Med Baghdad. 2020; 62(1,2): 41–47.
21. Al-Imam A, Khalid U, Al-Doori HJ. Clustering Analysis of Coronavirus Disease 2019 Pandemic. Asian J Med Sci. 2020; 12(2): 108–113.
22. Al-Imam A, Khalid U, Al-Doori HJ. Predictive Epidemiology for SARS-CoV-2 Pandemic in Iraq. Asian J Med Sci. 2021; 12(3): 121–124
23. Schmider J, Kumar K, LaForest C, Swankoski B, Naim K, Caubel PM. Innovation in pharmacovigilance: use of artificial intelligence in adverse event case processing. Clin Pharmacol Ther. 2019; 105(4): 954–61.
24. Al-Imam A, Motyka MA, Al-Doori HJ. Surface Web Merits for SARS-CoV-2 Pandemic in Iraq. J Fac Med Baghdad. 2020; 62(4): 117–127.
25. Arora VS, McKee M, Stuckler D. Google Trends: Opportunities and limitations in health and health policy research. Health Policy. 2019; 123(3): 338–341.
26. Lund B, Beckstrom M. The Integration of Tor into Library Services: An Appeal to the Core Mission and Values of Libraries. Public Libr Q. 2021; 40(1): 60–76.
27. Vaughan L, Chen Y. Data mining from web search queries: A comparison of google trends and baidu index. J Assoc Inf Sci Technol. 2015; 66(1): 13–22.