Association of side effects of COVID-19 vaccines with respect to hypertension.

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ABSTARCT

Objective: Effectiveness and safety are essential for the progression of effective COVID-19 vaccines. The side effects of vaccines affect vaccine reluctance. Therefore, this study aimed to determine the prevalence, and onset of side effects following the first and second doses of COVID- 19 vaccines among hypertensive and non-hypertensive individuals.

Methodology: This was a multicenter, cross-sectional study that was conducted in different hospitals, using a non-probability sampling technique. The duration of the study was about six months, from August 1, 2022, to January 31, 2023.A total of 818 participants were divided into two groups: hypertensive (n=414) and normotensive or non-hypertensive (n=404) who received one of COVID-19 vaccines, such as Sinopharm, Sinovac, Astrazeneca, and Pfizer. The frequency of side effects was evaluated among hypertensive and non-hypertensive participants using the Chi-square test. An independent t-test was used to compare the association between means.

Results: The study findings showed that themean age of hypertensive participants was 47.7±14.0 years while the mean age of non-hypertensive participants was 39.04±14.6 years. Most participants received Sinovac,by 186(45.1%) hypertensive participants and 150(37.1%) non-hypertensive participants.Following the first dose, the risk of side effects was higher in hypertensive participants. Pain at the injection site was experienced by 251(60.6%) hypertensive and 170(42.1%) non-hypertensive participants, with a significant difference observed among

them, ($p<0.001$). Moreover, following the second dose, redness at injection site, lymphadenopathy, headache, nausea, flu, anxiety, fatigue, swelling of glands, shortness of breath, and chest pain were significantly associated with both groups ($p<0.001$).

Conclusion: This study concluded that hypertension is a common comorbidity in COVID-19 individuals and is linked with greater reported side effects after vaccination in participants with hypertensio. Fever, discomfort, and burning at the injection site were the most frequent side effects after the first dose, and were more pronounced in participants with hypertension. Additionally, pain at the injection site, rashes, and fever were the most common side effects after the second dose.

Keywords: COVID-19 vaccines, hypertension, side effects, pain, fever

INTRODUCTION

The SARS-CoV-2 virus that causes the coronavirus disease 2019 (COVID-19) ravaged the globe starting in late 2019 and was formally recognized as a pandemic by the World Health Organization (WHO) in March of 2020. New and more transmissible varieties of the virus have developed, and the illness continues to pose a serious concern because of the continuing spread of the virus over the world, particularly among unvaccinated populations.Diabetes and advanced age are two risk variables linked to severe disease that have been found in previous studies [1,2]. Poorer results have also been connected to hypertension [3-5]. Around, 1.13 billion people worldwide have been diagnosed with hypertension, and this number exceeds 108 million in the US alone [6–8]. Numerous studies from all across the world have shown links between hypertension and the chance of developing severe COVID-19, along with higher rates of hospitalization and the requirement for respiratory support [9–11]. Consequently, old age along with existence of comorbidities have been linked with poor outcomes in hospitalized COVID-19 patients [12]. Emerging findings demonstrated that diabetes mellitus, hypertension, cardiac dysfunction [coronary heart disease (CHD), congestive heart failure (CHF)] and chronic kidney disease were major risk factors that could influence the clinical manifestations and prognosis in patients with COVID-19 [13,14].

According to recent findings, numerous symptoms (including pyrexia, cough, breathlessness, muscle aches, and lethargy) can be used to identify the new Corona virus [15,16]. SARS-CoV-2 or COVID-19 can spread through the respiratory tract, just like other viral respiratory illnesses. It primarily causes respiratory tract infections, and infected patients who develop severe pneumonia may need critical care. A serious illness may cause death from gradual respiratory failure [17,18]. Although this virus can affect anyone, elderly people and people with underlying medical conditions are more likely to have negative effects. According to existing knowledge, individuals with underlying chronic conditions have a higher death risk [19].

Before vaccines became available in 2021, COVID-19 preventative measures and control strategies in the community based on a complementary set of non-pharmacological interventions, such as hygiene practices, the use of personal safety equipment, social distancing, crowd restrictions, community lockdowns, and travelling bans [20]. The COVID-19 vaccines enabled effective therapy, decreasing COVID-19-related sickness and hospitalization, potentially modifying the pandemic's trajectory and its effects [21]. According to reports, typical vaccination side effects include injection site pain and soreness, fever, muscle aches, tiredness, and headache [22]. The low occurrence of serious adverse events may indicate that immunizations are relatively safe. Hence, public acceptance is necessary for vaccine uptake. There is still a need to look into and record safety data for COVID-19 vaccines in various settings because of enduring issues including public skepticism and limited acceptance even among healthcare professionals [23].

The majority of global efforts to control COVID-19 rely on people taking safety measures to lower the likelihood of viral transmission [24]. In the fight against COVID-19, a variety of medications and therapeutic substances have been suggested, however these only serve as supporting therapies [25]. The most effective preventive tool for a successful public health response is likely to continue to be vaccination [26]. By producing antibodies that will guard against potential diseases in the future, vaccines stimulate the body's adaptive immune response. Effective vaccinations can lower illness morbidity, mortality, and the spread of the disease, as well as provide protective immunity [27,28]. It is crucial for vaccine recipients, professionals, and caregivers to be aware of potential side effects [29]. Information on the prevalence of

common chronic diseases is still scarce. Furthermore, it is crucial for the people to understand the underlying illnesses in COVID-19-infected patients. Therefore, the aim of this study was to determine the prevalence, and onset of side effects following the first and second doses of COVID- 19 vaccines among hypertensive and non-hypertensive individuals.

METHODOLOGY

This was a multicenter, cross-sectional study that was conducted in different hospitals, using a non-probability sampling technique. The duration of the study was about six months, from August 1, 2022, to January 31, 2023. The ethical approval was obtained by the Ethical Review Committee. A total of 818 participants were divided into two groups: hypertensive (n=414) and normotensive or non-hypertensive (n=404) who received one of COVID-19 vaccines, such as Sinopharm, Sinovac, Astrazeneca, and Pfizer (double doses or booster doses), were included in the study. While the non-vaccinated individuals were excluded from the study.

A self-designed questionnaire was used to gather the participants' information. Demographic details of participants such as gender, age, co-existing diseases, vaccine type and doses, previous exposure to COVID-19 infection, and the incidence of any systemic and local side effects following receiving the 1^{st} and 2^{nd} doses of vaccines were documented. Participants' levels of satisfaction were also documented. Participants were considered hypertensive if their systolic blood pressure (SBP) was greater than 130 mmHg and their diastolic blood pressure (DBP) was lower than 80 mmHg. All of the other individuals with normal blood pressure and no prior use of antihypertensive medicines at home represented the normotensive group.

Data was analyzed using SSPS version 20.0. By using means, standard deviation, frequencies, and percentages, different demographic factors (sex, age, vaccine type, number of doses, and local and systemic side effects) were compared. The frequency of side effects was evaluated among hypertensive and non-hypertensive participants using the Chi-square test. An independent t-test was used to compare the association between means. A p value of < 0.05 was considered statistically significant.

RESULTS

A total of 818 participants, with 414 (or 50.6%) being hypertensive and 404 (or 49.4%) being non-hypertensive after receiving COVID-19 vaccines, were included in the study. In the hypertensive group, 224(54.1%) were males and 190(45.9%) were females, whereas in the non-hypertensive group, 206(51.0%) were males and 198(49.0%) were females. The mean age of hypertensive participants was 47.7±14.0 years and the mean age of non-hypertensive participants was 39.04±14.6 years with a significant difference between them, (p=0.004). The mean weight of hypertensive participants was 75.61±16.86 kg and mean weight of non-hypertensive participants was 64.22±14.81 kg with a significant difference between them, (p<0.001). The mean duration of hypertension was 4.93±4.161 years. Additionally, the mean duration of diabetes in the hypertensive group was 3.98±2.69 years, and it was 3.97±4.11 years in the non-hypertensive group. Moreover, 135(32.6%) had diabetes in the hypertensive group, 74(18.3%) had diabetes in the non-hypertensive group, with an insignificant association between them, (p=0.372). Currently, the COVID-19 infection has infected 98 (23.7%) hypertensive group and 83 (20.5%) non-hypertensive group, with an insignificant association (p = 0.281). Additionally, 32(7.7%) hypertensive group and 20(5.0%) non-hypertensivegroup had previous exposure of COVID-19 infection, with an insignificant association between them, (p=0.103). In terms of type of injected vaccine, Sinopharm was received by 95(22.9%) hypertensive participants and 99(24.6%) non-hypertensive participants. Sinovac was received by 186(45.1%) hypertensive participants and 150(37.1%) non-hypertensive participants. Astrazeneca was received by 32(7.6%) hypertensive participants and 63(15.6%) non-hypertensive participants. Pfizer was received by 101(24.4%) hypertensive participants and 92(22.7%) non-hypertensive participants, with a significant association observed between all vaccines and both groups, (p=0.006). Approximately, 41(9.9%) hypertensive participants and 51(12.5%) non-hypertensive participants received the 1st and 2nd dose of vaccine, whereas 373(90.1%) hypertensive participants and 353(87.5%) non-hypertensive participants received the 1st and 2nd dose along with a booster dose of vaccine, although there was a significant association observed among them, (p=0.002), as shown in Table I.

Following the 1st dose, the risk of side effects was higher in hypertensive participants. Pain at the

injection site was experienced by 251(60.6%) hypertensive and 170(42.1%) non-hypertensive participants, with a significant difference observed among them, ($p<0.001$). With a significant difference ($p=0.002$), swelling at the injection site occurred in 204 (49.3%) hypertensive participants and 158 (39.1%) non-hypertensive participants. Fever was reported in 296(71.5%) hypertensive and 211(52.2%) non-hypertensive participants, with significant association observed between them, ($p<0.001$). Furthermore, burning at the injection site was felt by 259(62.6%) hypertensive and 170(42.1%) non-hypertensive participants with a significant difference between them, ($p<0.001$). Moreover, redness at the injection site, lymphadenopathy, headache, nausea, anxiety, muscle pain, joint pain, chills, cough, swelling of the glands, shortness of breath, and diarrhea were significantly associated with both groups ($p<0.001$). On the other hand, an insignificant association was observed between flu, fatigue, sore throat, and chest pain in both groups ($p>0.001$), as shown in Table II.

The distribution of side effects after the 2nddose of COVID-19 vaccine among the participants revealed that the most commonly observed side effect was pain at the injection site, which was felt by 213(51.4%) hypertensive and 157(38.9%) non-hypertensive participants, with a significant difference between groups ($p<0.001$). Swelling at injection site occurred in 188(45.4%) hypertensive and 139(34.4%) non-hypertensive participants, with a significant difference observed among them ($p=0.001$). Fever was reported in 194(46.9%) hypertensive and 153(37.9%) non-hypertensive participants, with a significant difference between groups ($p=0.009$. Furthermore, rashes developed in 209(50.5%) hypertensive and 120(29.7%) non-hypertensive participants, with a significant difference between groups ($p<0.001$). Moreover, redness at injection site, lymphadenopathy, headache, nausea, flu, anxiety, fatigue, swelling of glands, shortness of breath, and chest pain were significantly associated with both groups ($p<0.001$). On the other hand, an insignificant association was observed between burning at injection site, joint pain, chills, diarrhea, cough, and sore throat in both groups ($p>0.001$), as shown in Table III.

The majority of the hypertensive 232(56.0%) and non-hypertensive215(53.2%) participants were satisfied with their vaccination. While, only 8(1.9%) hypertensive participants and 10(2.5%) non-hypertensive participants were dissatisfied, there was a significant association observed between them ($p<0.001$), as shown in Table IV.

Table I: The participants' basic demographic characteristics (n=818).

Variable		Hypertensive Mean±SD n(%)	Non-Hypertensive Mean±SD n(%)	p-value
Age (years)		47.7±14.0	39.04±14.6	0.004
Weight (kg)		75.61±16.86	64.22±14.81	<0.001
Hypertension Duration (years)		4.93±4.161	---	--
Diabetes Mellitus Duration (years)		3.98±2.69	3.97±4.11	--
Gender	**Male**	224(54.1%)	206(51.0%)	0.372
	Female	190(45.9%)	198(49.0%)	
Diabetes Mellitus	**Yes**	135(32.6%)	74(18.3%)	--
	No	279(67.4%)	330(81.7%)	
COVID-19 Infection	**Yes**	98(23.7%)	83(20.5%)	0.281
	No	316(76.3%)	321(79.5%)	
Previous COVID-19 Exposure	**Yes**	32(7.7%)	20(5.0%)	0.103
	No	382(92.3%)	384(95.0%)	
Type of vaccine	**Sinopharm**	95(22.9%)	99(24.6%)	0.006
	Sinovac	186(45.1%)	150(37.1%)	
	Astrazeneca	32(7.6%)	63(15.6%)	
	Pfizer	101(24.4%)	92(22.7%)	
Vaccination status	**Vaccinated with 1st and 2nd dose**	41(9.9%)	51(12.5%)	0.002
	Vaccinated with Booster Dose	373(90.1%)	353(87.5%)	

Table II: The distribution of side effects of COVID-19 vaccine after 1st dose of COVID-19 vaccine among the hypertensive and non-hypertensive participants.

Variable	Hypertensive		Non-Hypertensive		p-value
	Yes n(%)	No n(%)	Yes n(%)	No n(%)	
Pain at injection site	251(60.6%)	163(39.4%)	170(42.1%)	234(57.9%)	<0.001
Swelling at injection site	204(49.3%)	210(50.7%)	158(39.1%)	246(60.9%)	0.002
Redness at injection site	116(28.0%)	298(72.0%)	66(16.3%)	338(83.7%)	<0.001
Lymphadenopathy	151(36.5%)	263(63.5%)	82(20.3%)	322(79.7%)	<0.001
Fever (temperature >37.8 ˚C)	296(71.5%)	118(28.5%)	211(52.2%)	193(47.8%)	<0.001
Headache	139(33.6%)	275(66.4%)	88(21.8%)	316(78.2%)	<0.001
Nausea	79(19.1%)	335(80.9%)	38(9.4%)	366(90.6%)	<0.001
Rashes	135(32.6%)	279(67.4%)	118(29.2%)	286(70.8%)	0.164
Burning at injection site	259(62.6%)	155(37.4%)	170(42.1%)	234(57.9%)	<0.001
Flu	77(18.6%)	337(81.4%)	62(15.3%)	342(84.7%)	0.126
Anxiety	137(33.1%)	277(66.9%)	94(23.3%)	310(76.7%)	0.001
Muscle pain (Myalgia)	175(42.3%)	239(57.7%)	109(27.0%)	295(73.0%)	<0.001
Fatigue	124(30.0%)	290(70.0%)	115(28.5%)	289(71.5%)	0.640
Joint pain	188(45.4%)	226(54.6%)	128(31.7%)	276(68.3%)	<0.001
Chills	172(41.5%)	242(58.5%)	128(31.7%)	276(68.3%)	0.003
Cough	148(35.7%)	266(64.3%)	66(16.3%)	338(83.7%)	<0.001
Swelling of glands	121(29.2%)	293(70.8%)	82(20.3%)	322(79.7%)	0.003
Sore throat	130(31.4%)	284(68.6%)	124(30.7%)	280(69.3%)	0.827
Shortness of breath	178(43.0%)	236(57.0%)	76(18.8%)	328(81.2%)	<0.001
Diarrhea	98(23.7%)	316(76.3%)	68(16.8%)	336(83.2%)	0.015
Chest Pain	95(22.9%)	319(77.1%)	88(21.8%)	316(78.2%)	0.689

Table III: The distribution of side effects of COVID-19 vaccine after 2nd dose of COVID-19 vaccine among the hypertensive and non-hypertensive participants.

Variable	Hypertensive		Non-Hypertensive		p-value
	Yes n(%)	No n(%)	Yes n(%)	No n(%)	
Pain at injection site	213(51.4%)	201(48.6%)	157(38.9%)	247(61.1%)	<0.001
Swelling at injection site	188(45.4%)	226(54.6%)	139(34.4%)	265(65.6%	0.001
Redness at injection site	82(19.8%)	332(80.2%)	34(8.4%)	370(91.6%)	<0.001
Lymphadenopathy	145(35.0%)	269(65.0%)	110(27.2%)	294(72.8%)	0.016
Fever (temperature >37.8 ˚C)	194(46.9%)	220(53.1%)	153(37.9%)	251(62.1%)	0.009
Headache	145(35.0%)	269(65.0%)	104(25.7%)	300(74.3%)	0.004
Nausea	24(5.8%)	390(94.2%)	12(3.0%)	392(97.0%)	0.049
Rashes	209(50.5%)	205(49.5%)	120(29.7%)	284(70.3%)	<0.001
Burning at injection site	177(42.8%)	237(57.2%)	164(40.6%)	240(59.4%)	0.531
Flu	90(21.7%)	324(78.3%)	64(15.8%)	340(84.2%)	0.031
Anxiety	135(32.6%)	279(67.4%)	92(22.8%)	312(77.2%)	0.002
Muscle pain (Myalgia)	190(45.9%)	224(54.1%)	130(32.2%)	274(67.8%)	<0.001
Fatigue	148(35.7%)	266(64.3%)	84(20.8%)	320(79.2%)	<0.001
Joint pain	143(34.5%)	271(65.5%)	126(31.2%)	278(68.8%)	0.307
Chills	119(28.7%)	295(71.3%)	132(32.7%)	272(67.3%)	0.223
Cough	56(13.5%)	358(86.5%)	42(10.4%)	362(89.6%)	0.168
Swelling of glands	187(45.2%)	227(54.8%)	126(31.2%)	278(68.8%)	<0.001
Sore throat	56(13.5%)	358(86.5%)	70(17.3%)	334(82.7%)	0.132
Shortness of breath	185(44.7%)	229(55.3%)	108(26.7%)	296(73.3%)	<0.001
Diarrhea	90(21.7%)	324(78.3%)	74(18.3%)	330(81.7%)	0.222
Chest Pain	153(37.0%)	261(63.0%)	90(22.3%)	314(77.7%)	<0.001

Table IV: Association of level of satisfaction for vaccine with respect to hypertensive and non-hypertensive participants.

Variable		Hypertensive	Non Hypertensive	p-value
Overall subject level of Satisfaction for vaccine	**Very Satisfied**	41(9.9%)	109(27.0%)	<0.001
	Satisfied	232(56.0%)	215(53.2%)	
	Don't know	133(32.1%)	70(17.3%)	
	Dissatisfied	8(1.9%)	10(2.5%)	

DISCUSSION

The COVID-19 pandemic's exceptional and deadly problems and record-breaking efforts to create and distribute vaccinations as well as widespread interest in the efficient, quick manufacture of safe vaccines. Vaccines are made to stimulate the immune system (reactogenicity). Within a few days of vaccination, these mechanisms are frequently linked to brief post-vaccination side effects include soreness at the injection site, temperature, and fatigue [30]. But occasionally, serious adverse effects can also happen [31]. The perception and level of activation of immune system are modulated by a number of variables, including host and vaccine features and the route of vaccination administration [32].This study demonstrated the reported side effects following COVID-19 vaccinations among hypertensive and normotensive persons.

One of the cross-sectional study conducted in India, 40% of the participants reported experiencing at least one side effect after receiving the first dose of the COVID-19 vaccination. The Covishield vaccine (AstraZeneca) was administered to more than 91% of the responders, and the most frequent side effects were pain at the injection site, followed by tenderness of the injected arm (78.9%), fatigue (71.1%), fever (54.9%), and headache in 49.8% responders. The majority of the early immunization-related symptoms were minor and were disappeared within three days [33]. Similar findings were found in recent Indian investigations, which found that HCWs reported adverse effects at rates ranging from 40% to 70% [34–37]. Additional research in India [38] and other Asian nations [29, 39] has shown that common negative effects of the

COVID-19 vaccination include fever, tiredness, myalgia, joint pain, and headache. These findings were inconsistent with the findings of the present study, which reported that most of the participants were vaccinated by Sinovac, followed by Sinopharm.Fever was the most prevalent side effect observed following first dose of vaccines, followed by burning at the injection site among hypertensive and non-hypertensive participants, with significant difference observed among them ($p<0.001$). However, headache was also significantly reported among hypertensive and non-hypertensive individuals ($p<0.001$). Additionally, pain at the injection site was the most commonly observed side effect following second dose of vaccines, followed by rashes and fever.

An Indian research evaluated the side effects after receiving the first dosage of Covishield and Covaxin [33]. The most frequently reported side effect was pain at the injection site, which was in line with previous findings. Most people stated in another study that adverse effects were minor and self-limiting [40], Their conclusions that the reported side effects were minor to moderate, self-limiting, and did not require further treatment are supported by the clinical trial results that are currently available for several COVID-19 vaccinations. [41-43] [41] Similar to other studies on HCWs conducted in Bangladesh, India, [36,37] Nepal [41], and other countries, [29] the majority of respondents (93.4%) reported mild to moderate symptoms that were self-limiting and disappeared in a few days. The present study was partially consistent with the above mentioned studies and revealed that fever 296(71.5%) was the most commonly reported side effect following the first dose of vaccines, whereas pain 213(51.4%) was the most prevalent side effect following the second dose of vaccines, in hypertensive participants. Moreover, these symptoms were mild enough in severity that they required no treatment to resolve.

Likewise, another cross-sectional study conducted in Iran, explored the side effects of the most frequently injected COVID-19 vaccines such as Sinopharm, Sputnik V, and AstraZeneca vaccines. About 4775 individuals who received the vaccine in both doses were included in the study. Fatigue 1355(28.3%), chills and fever 1283(26.8%), and musculoskeletal pain 1069(22.3%) were the symptoms that were most frequently reported in 72 hours after the initial dose. The top three symptoms were the same for the first 72 hours following the second dose. But the distribution and occurrence were different: 536 (11.2%) had chills and fever, 582 (12.2%) had musculoskeletal pain, and 793 (16.6%) had overall fatigue. The total number of symptoms was significantly reduced during the first 72 hours post injection; it was 42 after the

second dose, compared to 157 participants for the first dose [44]. According to the present study, the most common side effects reported after the first dose were pain at the injection site 251(60.6%), fever 296(71.5%), and joint pain 188(45.4%), chills 172(41.5%), and general fatigue 124(30.0%). whereas it was less reported after the second dose of vaccines. In terms of vaccine type, Sinovac 186 (45.1%) was the most commonly injected vaccine in the majority of participants.

On social media, a lot of unproven accusations about alleged negative effects have gone around [45]. Despite the lack of proof for a causative link, multiple cases of death following vaccination have been reported in the public and on social media [46]. Although few vaccines have been related to deaths in rare instances, evidence for the COVID-19 vaccines that are now on the market shows no immediate major adverse effect concerns. In a previous study, researchers discovered a few rare but serious side effects among Bangladeshi physicians who had received the first dose of the Covishield (AstraZeneca) vaccination. These included meningismus, severe eye discomfort, irregular menstruation, heavy menstrual bleeding, and blood in urine [29]. The present study was not in agreement with the above-reported findings and revealed that no cases of serious adverse events were observed.

This study had some limitations. The potential participants' motivation or capacity to reply to the survey may have been influenced by the occurrence of adverse effects. The use of probability sampling in future studies might be beneficial. Finally, we advise that the absence of serious adverse effects right after immunization does not guarantee vaccine safety in the long run. The direct comparison of COVID-19 participants with hypertension and non-hypertension at the same time and location is a strength of this study.

CONCLUSION

This study concluded that hypertension is a common comorbidity in COVID-19 individuals and is linked with greater reported side effects after vaccination in participants with hypertension as compared to participants without hypertension. Fever, discomfort, and burning at the injection site were the most frequent side effects after the first dose, and were more pronounced in participants with hypertension. Additionally, pain at the injection site, rashes, and fever were the most typical side effects after the second dose. In particular, after booster doses, more thorough

studies are required to assess the potential long-term side effects of COVID-19 vaccinations and ascertain their true prevalence. These studies must be done in order to address attitudes about vaccine hesitancy and boost vaccination rates.

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