A Cross-Sectional Study on Post COVID-19 Vaccination Adverse Effects in the Diabetic and Non-Diabetic Population

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A Cross-Sectional Study on Post Covid19 Vaccination Adverse Effects in The Diabetic and Non-Diabetic Population

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Dedicated to

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LIST OF ACRONYMS

SARS-COV-2	Severe acute respiratory syndrome coronavirus 2
LDL	Low-density Lipids
HDL	High-density Lipids
TG	Triglycerides
CRP	C Reactive Protein
HbA1C	Hemoglobin A1C
TSH	Thyroid Stimulating Hormone
WHO	World Health Organization
SPSS	Statistical Package for Social Sciences

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ABSTRACT

Vaccination was the only method available to stop the COVID-19 epidemic once it had started. There is skepticism about the efficacy and safety of current COVID-19 vaccination around the world. Because glycemic alterations have been observed after immunization, there were significant worries regarding post-vaccination unfavorable consequences in the diabetic community. The purpose of this study is to examine the adverse effects of post-COVID-19 vaccination in diabetic and non-diabetic subjects who received various types of vaccinations, including inactivated viral vaccines (Sinopharm and Sinovac), RNA-based vaccines (Moderna and Pfizer), and non-replicating-viral vaccines (AstraZeneca and Casino bio). This study aims to investigate the concomitant side effects caused by different COVID-19 vaccines in diabetic and non-diabetic populations by questionnaire, interviews, and analysis of blood samples for different biomarkers. Data collected was analyzed using IBM-SPSS by applying an independent sample T-test, chi-square test, and binary logistic regression. Most of the side effects were reported within the age group 31-40 and 41-50. There is no significant difference in side effects after vaccination in diabetic and non-diabetic individuals. The glycemic imbalance was seen high in individuals vaccinated with RNA-based vaccine with n=27(31.2%) reporting high blood sugar levels. Concluded that these vaccines are safe for diabetic individuals but keeping results in view RNA-based vaccines should be administered with blood glycemic levels in check.

Keywords: COVID-19 vaccination, side effects of vaccination, diabetes

CHAPTER 1

INTRODUCTION

1. INTRODUCTION

An absolute or relative shortfall in insulin synthesis or action results in hyperglycemia, which is the hallmark of the varied group of illnesses known as diabetes mellitus. Type 1 and type 2 diabetes mellitus are the two main subtypes of the disease, and their respective treatments are decided by etiopathology. Despite being a global health concern, there are significant regional differences in the treatment of diabetes mellitus, especially in the availability of essentials like insulin [1].

The global public health emergency known as COVID-19, which is caused by the SARS-CoV-2 infection, has spread quickly around the world. Both SARS-CoV-2 and SARS-CoV are SARS-like species that belong to separate clusters in the subfamily *Coronavirinae* of the family *Coronaviridae* of the order *Nidovirales* [2]. In addition, there are differences in viral structure, epidemiological traits, and pathogenic traits.

According to the CDC, most potential symptoms of COVID-19 infection include Fever or chills, cough, shortness of breath or difficulty breathing, fatigue, muscle or body aches, headache, loss of taste or smell, sore throat, congestion or runny nose, nausea, or vomiting.

1.1 Statistics of Diabetes in Pakistan

With a 30.8% age-adjusted prevalence of adults with diabetes (20-79 years), Pakistan is expected to lead the list of nations in 2021. 33 million persons in the United States (20-79 years old) have diabetes. In Pakistan, there is a reported prevalence of 26.7%, with one in four persons having diabetes. In Pakistan, the

prevalence of undiagnosed diabetes is 26.9%. 396,625 people have died as a result of diabetes [3].

1.2 Statistics of COVID-19 in Pakistan

As of the end of August 2022, there were around 603 million confirmed cases in the country, up from the original two instances on February 26, 2020. By August 31st, 2022, there will have been 6.47 million deaths worldwide. In Pakistan, 131 M (59.5%) people have had all their vaccinations.

1.3 COVID-19 Vaccination

When creating a vaccination, there are three main methods. They differ depending on whether they use a complete virus or bacterium, simply the immune system-stimulating components of the germ, or just the genetic material that contains the instructions for producing particular proteins rather than the entire virus.

Inactivated viral vector vaccines use chemicals, heat, or radiation to inactivate or kill the disease-causing virus, bacteria, or a very close relative. It contains the vaccinations Sinopharm and Sinovac. A live and attenuated viral vaccine including weakened strain of the virus—or one very similar to it—is used in a live-attenuated vaccine. This method is scalable and uses technology comparable to the inactivated vaccine. These vaccines, however, might not be suitable for those with weakened immune systems. This category includes CanSino bio and AstraZeneca. A viral vector vaccine uses a secure virus to transfer particular pieces, or proteins, of the target germ in order to elicit an immune response without actually transmitting illness. To do this, a safe virus is modified to contain the instructions for creating certain components of the pathogen of interest. A nucleic acid vaccine, as opposed to other vaccine methods, only employs the portion of the microbe's

genetic code that contains the instructions for particular proteins, not the entire organism. Our cells follow the instructions in DNA and RNA to create proteins for example Pfizer and Moderna [4].

1.4 Side Effects of Vaccination

These regulations aim to immunize people who are most likely to get COVID-19, get hospitalized for it, or perhaps pass away from it. linked with an increased case fatality rate in COVID-19 cases (obesity, diabetes, and hypertension). Greater COVID-19 morbidity and mortality have been reported in several clinical reports in individuals with diabetes, who are frequently obese. Less is known about the risk of type 1 diabetes; a phenotypically different condition and the majority of this knowledge comes from people with type 2 diabetes. Patients with type 1 diabetes and type 2 diabetes both exhibited roughly identical adjusted odds ratios (ORs) for hospitalization [5].

According to published data, vaccination often offers some advantages in lowering the risk of serious SARS-CoV-2 illness and death. Fear of the vaccine's negative side effects is one of the primary variables connected to vaccination readiness for COVID-19 [6].

The most common side effects reported after vaccination in previous literature are fever and chills, pain at the site of injection, arthritis, headache, muscle ache, diarrhea, vomiting, hyperglycemia, hypoglycemia, bradycardia, tachycardia, hypertension, hypotension, chest pain, and loss of sense of smell and taste [7]. There are several case studies that report hyperglycemic conditions after vaccination. Ketosis predominance and exceptionally high insulin needs are suggestive of severe insulin resistance, disproportionate to that found in the

context of critical illness more generally. Clinical and pathophysiological characteristics are still poorly understood.

1.5 Aims and Objectives

Objectives of this study includes:

- This study aims to evaluate major post-vaccination side effects in diabetic and non-diabetic patients.
- To compare the intensity and frequency of biomarkers in the blood of the post-vaccinated diabetic vs nondiabetic population.
- Identify type of vaccines most suitable for diabetic set of population.

1.6 Literature Review

There is currently a lot of study being done on the post-vaccination adverse effects, including hyperglycemia condition reported after vaccination, and there have been multiple studies done over the last 3 years as covid 19 immunization is a recent phenomenon after covid 19 pandemic. However, there are many features of the COVID-19 vaccine that remain unknown. However, certain cross-sectional, retrospective observational, and case report studies are mentioned below.

1.7 Related Literature

There was considerable hesitation in Pakistan regarding the administration of vaccines due to many uncertainties regarding vaccine adverse effects and societal, cultural, and religious beliefs. Notably, those with comorbid conditions are already present.

P. Barbara *et al.* stated that the COVID-19 vaccine does not significantly affect glycemic control in adolescents and young adults with T1D and that, if an increase in glucose levels does occur, it is moderate, temporary, tolerated, and does not need adjusting insulin dosage [8]. H. Omeish *et al.* showed in the Jordanian population, there was a substantial increase (P .001) in the proportion of females (83%) who experienced pain at the injection site following the first dose of immunizations compared to males (70.4%) [9].

It is stated by Duan L. *et al.* that the COVID-19 immunization behavior of diabetes responders was inversely correlated with worries about the COVID-19 vaccine's safety and potential side effects (perceived impairment). 365 people in total had diabetes-related comorbidities, 56.4% (n = 364) of respondents had a family history of the disease, 31.0% (n = 200) of respondents had had the diagnosis for

more than 10 years, 6.5% of respondents indicated that their fasting blood sugar was above 13.9 mmol/L, and nearly 50% of respondents said that their most recent test showed a postprandial blood sugar of above 11.1 mmol/L [10].

A study done by Rizwan W. *et al.* states that participants with a prior COVID-19 infection had a higher incidence of adverse effects. Out of 225 respondents who had previously been infected, 97 (43.1%) (p-value = 0.020) and 90 (40%) (p-value = 0.001) experienced side effects following the first and second doses, correspondingly [11].

According to Edwards AE et al., all patients developed hyperglycemia despite having significantly increased HbA1c values [12]. Aberer, F. *et al.* showed that the COVID-19 vaccine itself had no effect on the glycemic management of diabetics. It should be noted that type 1 diabetics' glycemia deteriorated on days when adverse symptoms were evident [13].

There were no anaphylactic or urticaria reactions reported. After the first and second doses, 5 (1.0%) and 13 (2.6%) of the participating patients respectively, reported a perceived worsening of glucose control reported by Dicembrini, I. *et al.* [14].

CHAPTER 2

METHODS & MATERIALS

2. METHODS & MATERIALS

2.1 Hypothesis

Following is the hypothesis for this study.

•H1: There is a significant increase in side effects of vaccination in diabetic as compared to nondiabetic individuals.

•H0: There is no significant increase in side effects of vaccination in diabetic as compared to nondiabetic individuals.

Sub hypothesis:

H1a: There is a significant increase in post-vaccination blood glucose levels in diabetic as well as in non-diabetic individuals.

H0a: There is no significant increase in post-vaccination blood glucose levels in diabetic as well as in non-diabetic individuals.

2.2 Study design

A cross-sectional analysis of people with diabetes mellitus was conducted in this study. The study was carried out between December 2021 and February 2022 at the Hanif Medical Complex in Rawalpindi, Pakistan, in the outpatient clinic for the diabetic department.

2.3 Questionnaire

The questionnaire, which was developed in accordance with standards, also received assistance from statisticians. The study's prerequisites were examined to make sure they were all satisfied. The following demographic information was gathered: gender,

age, and location. Included clinical information includes the type of diabetes, the type of COVID-19 immunization, the date of vaccination, comorbidities, glycemic control, current medications, and other information. This study only accepts individuals who have received all necessary vaccinations. A checklist for post-vaccination side effects (such as pain at the injection site, myalgia, arthritis, fever, nausea, chest pain, fatigue, vomiting, diarrhea, allergic reaction, hypertension, and others) was kept for three weeks following the COVID-19 vaccination for the diabetic and non-diabetic set of samples.

2.4 Participants' Inclusion/Exclusion Criteria

The following individuals met the inclusion criteria: type 1 or type 2 diabetics, non-diabetics, between the ages of 20 and 60, willing to submit a written consent form for the survey, fully inoculated with COVID19 immunizations, and willing to provide blood samples for biomarker analyses. Patients without immunization records and those who were unvaccinated were excluded.

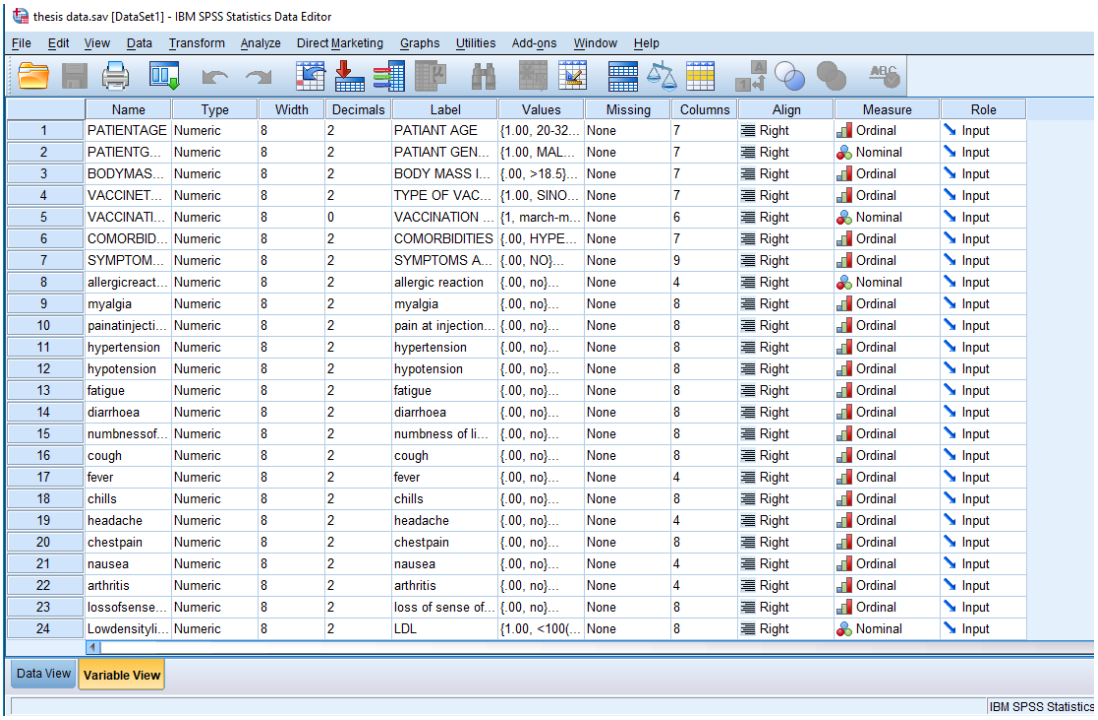
2.5 Permission from The Ethical Committee:

That documentation of the data had been done with the consent of the ethical committee of the Hanif medical hospital.

2.6 Data Collection

A written consent form was completed by interested candidates. Participants in the study filled out questionnaires, took part in in-person interviews, and gave appropriately labeled blood samples. There was a total of 438 eligible participants, however 17 people had partial surveys and 21 respondents declined to take part, therefore they were excluded. So, 400 volunteers—200 with and 200 without diabetes—gave their written consent, consented to the collection of blood samples, and

agreed to participate in interviews. Those who were eligible received no incentives. The hospital committee obtained instructions and ethical approval.



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2	PATIENTG...	Numeric	8	2	PATIANT GEN...	{1.00, MAL...	None	7	Right	Nominal	Input
3	BODYMAS...	Numeric	8	2	BODY MASS I...	{.00, >18.5}...	None	7	Right	Ordinal	Input
4	VACCINET...	Numeric	8	2	TYPE OF VAC...	{1.00, SINO...	None	7	Right	Ordinal	Input
5	VACCINATI...	Numeric	8	0	VACCINATION ...	{1, march-m...	None	6	Right	Nominal	Input
6	COMORBID...	Numeric	8	2	COMORBIDITIES	{.00, HYPE...	None	7	Right	Ordinal	Input
7	SYMPTOM...	Numeric	8	2	SYMPTOMS A...	{.00, NO}...	None	9	Right	Ordinal	Input
8	allergicreact...	Numeric	8	2	allergic reaction	{.00, no}...	None	4	Right	Nominal	Input
9	myalgia	Numeric	8	2	myalgia	{.00, no}...	None	8	Right	Ordinal	Input
10	painatinjecti...	Numeric	8	2	pain at injection...	{.00, no}...	None	8	Right	Ordinal	Input
11	hypertension	Numeric	8	2	hypertension	{.00, no}...	None	8	Right	Ordinal	Input
12	hypotension	Numeric	8	2	hypotension	{.00, no}...	None	8	Right	Ordinal	Input
13	fatigue	Numeric	8	2	fatigue	{.00, no}...	None	8	Right	Ordinal	Input
14	diarrhoea	Numeric	8	2	diarrhoea	{.00, no}...	None	8	Right	Ordinal	Input
15	numbnessof...	Numeric	8	2	numbness of li...	{.00, no}...	None	8	Right	Ordinal	Input
16	cough	Numeric	8	2	cough	{.00, no}...	None	8	Right	Ordinal	Input
17	fever	Numeric	8	2	fever	{.00, no}...	None	4	Right	Ordinal	Input
18	chills	Numeric	8	2	chills	{.00, no}...	None	8	Right	Ordinal	Input
19	headache	Numeric	8	2	headache	{.00, no}...	None	4	Right	Ordinal	Input
20	chestpain	Numeric	8	2	chestpain	{.00, no}...	None	8	Right	Ordinal	Input
21	nausea	Numeric	8	2	nausea	{.00, no}...	None	4	Right	Ordinal	Input
22	arthritis	Numeric	8	2	arthritis	{.00, no}...	None	4	Right	Ordinal	Input
23	lossofsense...	Numeric	8	2	loss of sense of...	{.00, no}...	None	8	Right	Ordinal	Input
24	Lowdensityli...	Numeric	8	2	LDL	{1.00, <100(...	None	8	Right	Nominal	Input

Figure 1 Data collection sheet on SPSS

2.7 Statistical Analysis

Calculated descriptive statistics included frequencies and percentages. Independent sample t-tests are used to determine the mean and standard deviation for continuous data, whereas chi-square tests are used to determine connections between factors for categorical variables. P 0.05 is used in the analysis to define statistical significance. A chi-square test was used to determine the significance of the disparity between diabetes and non-diabetic individuals when additional variables of interest were considered in order to analyze the adverse effects encountered post-COVID-19 vaccination. The chi-square test was used to compare the variation in biomarker levels among the various vaccine types, and the odds ratio was computed. A p-value of 0.05 or less was regarded as statistically significant when using SPSS 21 for the statistical analysis.

2.8 Blood Samples Analysis

The SMME, NUST lab used the necessary kits for investigations of biomarkers to analyze blood samples taken from diabetic and non-diabetic individuals for Low-Density Lipids, High-Density Lipids, creatinine, Thyroid Stimulating Hormone, HbA1C, Triglycerides, Alanine Transaminase, D dimer, and C Reactive Protein.

CHAPTER 3

RESULTS

3. RESULTS

3.1. Descriptive Statistics

These are descriptive statistics of data collected. This includes demographic variables such as age, gender, region, and comorbidities. Table 1 presents in frequency and percentages.

Table 1 : Descriptive statistics of demographic variables

Variables		**f**	%	M	S. D
PATIENT AGE	20-30	58	14.5	2.542	.9489
	31-40	139	34.8		
	41-50	131	32.8		
	51-60	72	18.0		
Gender	MALE	196	49.0	1.510	.5005
	FEMALE	204	51.0		
Region	ISLAMABAD	179	44.8	1.557	.5072
	RAWALPINDI	219	54.8		
	ABBOTTABAD	2	.5		
Bm index	>18.5	21	5.3	1.712	.8583
	18.5-25	158	39.5		
	25-30	136	34.0		
	>30	85	21.3		
group	Diabetic	200	50.0	1.500	.5006
	Non- Diabetic	200	50.0		

Type of vaccine	INACTIVATED Viral vaccine	290	72.5	1.402	.7047
	RNA based vaccine	59	14.8		
	Non-replicating viral vaccine	51	12.8		
Vaccination Date	March-May 21	50	12.5	2.56	.943
	June-August 21	156	39		
	September-November 21	116	29		
	December 21-february 22	78	19.5		
Comorbidities	Hypertension	25	6.3	2.770	.7639
	Kidney problems	6	1.5		
	Heart patient	5	1.3		
	None	364	91		

3.2. Analysis On Continuous Variables

Table 2 Independent sample T test

Variable	Group	Mean	S. D	T	Sig.	CI=95%		d
						LL	UL	
Number of symptoms	Nondiabetic	2.26	1.855	.573	.56	-.267	.487	0.05
	Diabetic	2.15	1.982					
Patient age	Nondiabetic	2.20	.801	-13.18	.00	-1.200	-.889	1.09
	Diabetic	3.06	.783					
Body mass index	Nondiabetic	1.37	.739	-8.545	.00	-.830	-.519	0.85
	Diabetic	2.05	.837					

Table 2 shows that for N=400, diabetic individuals had high score with different age groups having (M=3.1850, S. D=.77055), as compare to normal individuals having (M=2.0200, S. D=.80176), however the difference, 1.165 with 95% CI [-1.311, -1.010] was statistically significant T (400) =-14.816, p=.000 and represent a large effect size, d=1.481604 calculated by Cohen's d.

3.3. Analysis of Side Effects in Both Groups

Table 3 Chi-square analysis/fisher exact analysis on both groups

N=400	Diabetic vs Nondiabetic					
		Nondiabetic	Diabetic	$\chi 2$	p	V
Allergic reaction	Yes	10(100%)	0(0.0%)	10.256	**0.002**	0.160
	No	190(48.7%)	200(51.3%)			
Myalgia	Yes	63(42.0%)	87(58.0%)	6.144	**0.013**	0.124
	No	137(54.8%)	113(45.2%)			
Pain at site of injection	Yes	90(45.9%)	106(54.1%)	2.561	0.133	0.080
	No	110(53.9%)	94(46.1%)			
Hypertension	Yes	15(62.5%)	9(37.5%)	1.596	0.292	0.063
	No	185(49.2%)	191(50.8%)			
Hypotension	Yes	18(94.7%)	1(5.3%)	15.969	**0.000**	0.200
	No	182(47.8%)	199(52.2%)			
Fatigue	Yes	63(54.8%)	52(45.2%)	1.477	0.135	0.061
	No	137(48.1%)	148(51.9%)			
diarrhea	Yes	28(84.8%)	5(15.2%)	17.472	**0.000**	0.209
	No	172(46.9%)	195(84.8%)			

Numbness of limbs	Yes	23(46.0%)	27(54.0%)	0.366	0.325	0.030
	No	177(50.6%)	173(49.4%)			
cough	Yes	9(75.0%)	3(25.0%)	3.093	**0.070**	0.088
	No	191(49.2%)	197(50.8%)			
Fever	Yes	71(49.0%)	74(51.0%)	0.097	0.418	0.016
	No	129(50.6%)	126(49.4%)			
Headache	Yes	8(50.0%)	8(50.0%)	0.000	**1.000**	0.000
	No	192(50.0%)	192(50.0%)			
Chest pain	Yes	3(100%)	0(0.0%)	3.023	0.124	0.087
	No	197(49.6%)	200(50.4%)			
Nausea	Yes	20(83.3%)	4(16.7%)	11.348	**0.001**	0.168
	No	180(47.9%)	196(52.1%)			
Arthritis	Yes	19(25.0%)	57(75.0%)	23.457	**0.00**	0.243
	No	181(55.9%)	143(44.1%)			
Loss of sense of smell/taste	Yes	14(66.7%)	7(33.3%)	2.463	0.08	0.078
	No	186(49.1%)	193(50.9%)			

Table 3 shows the chi square test results to find the association between side effects of COVID 19 vaccination and group variable (diabetic vs non-diabetic). Results revealed statistically significant relationship of diabetes with allergic reactions ($\chi 2$ =10.256, p=0.005, V= 0.160),myalgia ($\chi 2$ =6.144, p=0.013, V= 0.124), Hypotension ($\chi 2$

=15.969, p=0.000, V=0.200) diarrhea (χ2 =17.472 p=0.000 V=0.209), Nausea (χ2 =11.384 p=0.001 V=0.168), Nausea(χ2 =11.384 P=0.001 V=0.168) Arthritis (χ2 =23.457 P=0.00 V=0.243). The effect size for these variables lies in the small range (Pallent 2010). Moreover, the table above also indicates that there was no significant relationship of diabetes with pain at site of injection, hypertension, fatigue, numbness of limbs, cough, fever, chest pain, loss of sense of smell/taste. Hence results shows that allergic reactions, myalgia, Hypotension, diarrhea, Headache, Nausea, Arthritis are most prevalent symptoms in diabetic set of samples.

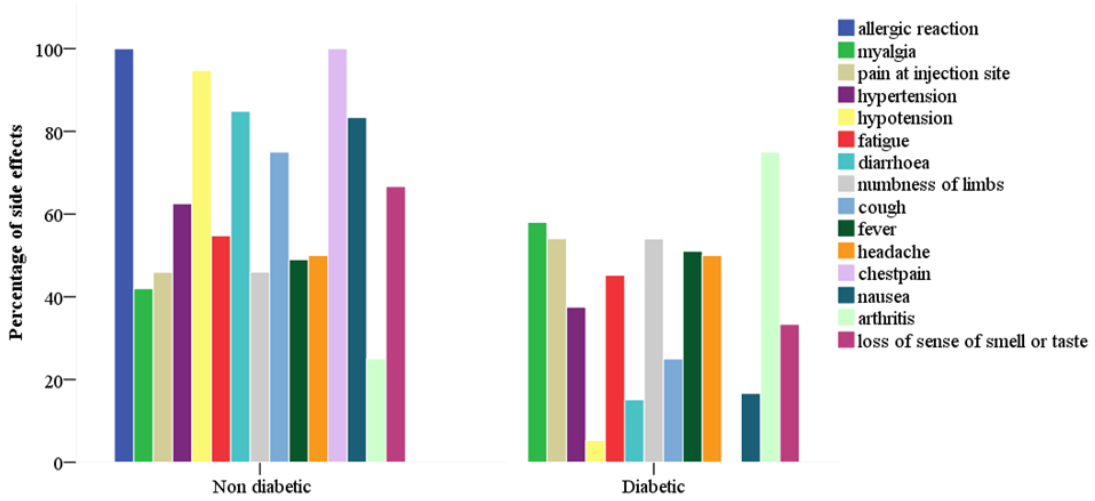

Figure 2 Comparison of side effects in both diabetic and non-diabetic groups

3.4. Analysis of Side Effects with the Type of Vaccination

Table 4 Chi-square analysis/fisher exact analysis on the type of vaccine and side effects

N=400		Type of vaccine					
		Inactivated viral vaccine	RNA based Vaccine	Non-Replicating Viral Vaccine	$\chi 2$	p	V
Allergic reaction	Yes	6(60.0%)	2(20.0%)	2(20.0%)	1.491	.44	0.04
	No	284(72.8%)	57(14.6%)	49(12.6%)			
Myalgia	Yes	113(75.3%)	18(12.0%)	19(12.7%)	1.498	.47	0.06
	No	177(70.8%)	41(16.4%)	32(12.8%)			
Pain at site of injection	Yes	155(79.1%)	25(12.8%)	16(8.2%)	9.674	.00	0.15
	No	135(66.2%)	34(16.7%)	35(17.2%)			
Hypertension	Yes	16(66.7%)	5(20.8%)	3(12.5%)	1.010	.62	0.70
	No	274(72.9%)	54(14.4%)	48(12.8%)			
Hypotension	Yes	14(73.7%)	3(15.8%)	2(10.5%)	0.139	1.0	0.01
	No	276(72.4%)	56(14.7%)	49(12.9%)			
Fatigue	Yes	86(74.8%)	13(11.3%)	16(13.9%)	1.586	.45	0.06
	No	204(71.6%)	46(16.1%)	35(12.3%)			
diarrhea	Yes	27(81.8%)	4(12.1%)	2(6.1%)	1.493	.46	0.06
	No	263(71.6%)	55(15.0%)	49(13.4%)			

Numbness of limbs	Yes	38(76.0%)	6(12.0%)	6(12.0%)	0.415	.86	0.03
	No	252(72.0%)	53(51.1%)	45(12.9%)			
cough	Yes	10(83.3%)	1(8.3%)	1(8.3%)	.304	.89	0.04
	No	280(72.8%)	58(14.9%)	50(12.9%)			
Fever	Yes	111(76.6%)	20(13.8%)	14(9.7%)	2.365	.30	0.07
	No	179(70.2%)	39(15.3%)	37(14.5%)			
Headache	Yes	13(81.3%)	2(12.5%)	1(6.3%)	5.708	.30	0.11
	No	277(72.2%)	57(14.8%)	50(13.0%)			
Chest pain	Yes	2(66.7%)	0(0.0%)	1(33.3%)	4.374	.42	0.10
	No	288(72.5%)	59(14.9%)	50(12.6%)			
Nausea	Yes	19(79.2%)	3(12.3%)	2(8.3%)	1.895	.88	0.06
	No	271(72.1%)	56(14.9%)	49(13.0%)			
Arthritis	Yes	60(78.9%)	10(13.2%)	6(7.9%)	2.434	.29	.078
	No	230(71.0%)	49(15.1%)	45(13.9%)			
Loss of sense of smell/taste	Yes	16(76.2%)	3(14.3%)	2(9.5%)	0.121	1.0	.024
	No	274(72.3%)	56(14.8%)	49(12.9%)			

Table 4 shows the chi-square test results to find the association between side effects of COVID-19 vaccination and the type of vaccination. Results revealed there is no statistically significant relationship between vaccine type with allergic reactions, myalgia, pain at site of injection, hypertension, hypotension fatigue, diarrhea,

numbness of limbs, cough, fever, chest pain, nausea, arthritis, loss of sense of smell/taste.

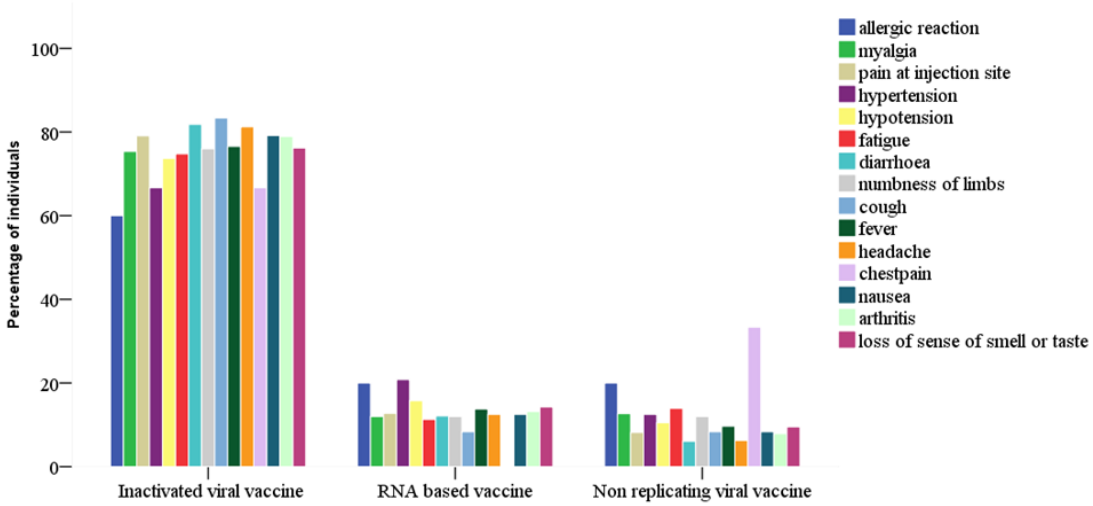

Figure 3 Side effects vs type of vaccination

3.5. Analysis of Side Effects with Patient Age

Table 5 Analysis of side effects with different age groups

N=400		Patient age						
		20-30	31-40	41-50	51-60	$\chi 2$	p	V
Allergic reaction	Yes	1(10%)	8(80%)	1(10%)	0(0%)	7.664	**0.02**	0.15
	No	57(14.6%)	131(33.6%)	130(33.3%)	72(18.5%)			
Myalgia	Yes	17(11.3%)	58(38.7%)	48(32.0%)	27(18.0%)	2.760	0.438	0.08
	No	41(16.4%)	81(32.4%)	83(33.2%)	45(18.0%)			
Pain at site of injection	Yes	26(13.3%)	71(36.2%)	70(35.7%)	29(14.8%)	3.868	0.278	0.09
	No	32(15.7%)	68(33.3%)	61(29.9%)	43(21.1%)			
Hypertension	Yes	5(20.8%)	7(29.2%)	10(41.7%)	2(8.3%)	2.886	0.400	0.08
	No	53(14.1%)	132(35.1%)	121(32.2%)	70(18.6%)			
Hypotension	Yes	2(10.5%)	11(57.9%)	6(31.6%)	0(0%)	7.072	**0.05**	0.13
	No	56(14.7%)	128(33.6%)	125(32.8%)	72(18.9%)			
Fatigue	Yes	12(10.4%)	52(45.2%)	38(33.0%)	13(11.3%)	10.935	**0.012**	0.16
	No	46(16.1%)	87(30.5%)	93(32.6%)	59(20.7%)			
diarrhea	Yes	7(21.2%)	12(34.4%)	12(34.4%)	2(6.1%)	4.136	0.210	0.10
	No	51(13.9%)	127(34.6%)	119(32.4%)	70(19.1%)			

Numbness of limbs	Yes	7(14.0%)	21(42.0%)	14(28.0%)	8(16.0%)	1.395	0.719	0.05
	No	51(14.6%)	118(33.7%)	117(33.4%)	64(18.3%)			
cough	Yes	2(16.7%)	3(25.0%)	6(50.0%)	1(8.3%)	1.964	0.614	0.07
	No	56(14.4%)	136(35.1%)	125(32.2%)	71(18.3%)			
Fever	Yes	17(11.7%)	52(35.9%)	58(40.0%)	18(12.4%)	8.883	**0.031**	0.14
	No	41(16.0%)	87(34.1%)	73(28.6%)	54(21.2%)			
Headache	Yes	2(12.5%)	5(31.3%)	5(31.3%)	4(25.0%)	.730	.908	0.03
	No	56(14.9%)	134(34.9%)	126(32.8%)	68(17.7%)			
Chest pain	Yes	0(0.0%)	2(66.7%)	1(33.3%)	0(0.0%)	1.295	0.776	0.06
	No	58(14.6%)	137(34.5%)	130(32.7%)	72(18.1%)			
Nausea	Yes	7(29.2%)	10(41.7%)	5(20.8%)	2(8.3%)	5.994	0.103	0.12
	No	51(13.6%)	129(34.3%)	126(33.5%)	70(18.6%)			
Arthritis	Yes	5(6.6%)	22(28.9%)	31(40.8%)	18(23.7%)	8.505	**0.036**	0.14
	No	53(16.4%)	117(36.1%)	100(30.9%)	54(16.7%)			
Loss of sense of smell/taste	Yes	4(19.0%)	7(33.3%)	7(33.3%)	3(14.3%)	.636	0.924	0.03
	No	54(14.2%)	132(34.8%)	124(32.7%)	69(18.2%)			

Table 5 shows the chi square test results to find the association between side effects of COVID 19 vaccination and age of individuals. Results revealed statistically significant relationship of age with allergic reactions ($\chi2$ =7.664, p=0.02, V= 0.155), Hypotension ($\chi2$ =7.072, p=0.050, V=0.131), fatigue ($\chi2$ =10.935, p=0.012, V= 0.165), fever ($\chi2$

=8.883 p=0.031, V=0.149), arthritis ($\chi 2$ =8.505, P=0.036, V=0.146). The effect size for these variables lies in the small range (pallent 2010). Moreover, the table above also indicates that there was no significant relationship of diabetes with myalgia, pain at site of injection, hypertension, diarrhea, numbness of limbs, cough, chest pain, nausea, loss of sense of smell/taste.

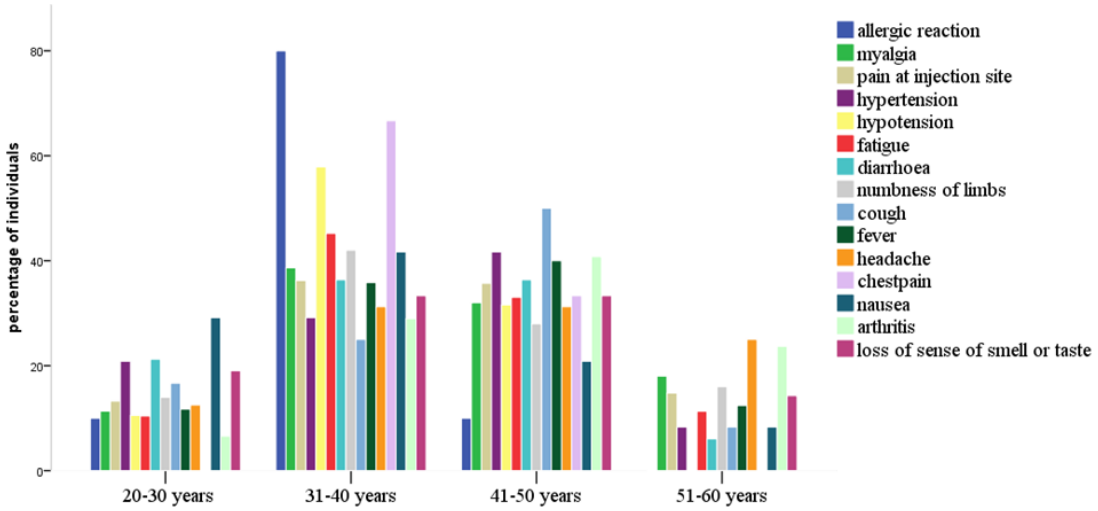

Figure 4 Side effects in different age groups

3.6. Analysis of Side Effects and Body Mass Index

Table 6 Chi-square analysis of body mass index and side effects

N=400		Body mass index						
		> 18.5	18.5-25	26-30	> 30	$\chi 2$	p	V
Allergic reaction	Yes	1(10.0 %)	5(50.0%)	4(40.0%)	0(0.0%)	3.015	.29	.08
	No	20(5.1 %)	153(39.2 %)	132(33.8 %)	85(21.8 %)			
Myalgia	Yes	7(4.7 %)	61(40.7 %)	48(32.0 %)	34(22.7 %)	.747	.87	.04
	No	14(5.6 %)	97(38.8 %)	88(35.2 %)	51(20.4 %)			
Pain at site of injection	Yes	11(5.6 %)	78(39.8 %)	59(30.1 %)	48(24.5 %)	3.720	.29	.09
	No	10(4.9 %)	80(39.2 %)	77(37.7 %)	37(18.1 %)			
Hypertension	Yes	1(4.2 %)	8(33.3%)	11(45.8 %)	4(16.7%)	1.607	.66	.06
	No	20(5.3 %)	150(39.9 %)	125(33.2 %)	81(21.5 %)			

Hypotension	Yes	3(15.8%)	11(57.9%)	3(15.8%)	2(10.5%)	8.954	**.030**	.15
	No	18(4.7%)	147(38.6%)	133(34.9%)	83(21.8%)			
Fatigue	Yes	6(5.2%)	51(44.3%)	37(32.2%)	21(18.3%)	1.798	.613	.06
	No	15(5.3%)	107(37.5%)	99(34.7%)	64(22.5%)			
diarrhea	Yes	2(6.1%)	19(57.6%)	10(30.3%)	2(6.1%)	7.07	.07	.13
	No	19(5.2%)	139(37.9%)	126(34.3%)	83(22.6%)			
Numbness of limbs	Yes	1(2.0%)	32(64.0%)	9(18.0%)	8(16.0%)	14.8	**.00**	.19
	No	20(5.7%)	126(36.0%)	127(36.3%)	77(22.0%)			
cough	Yes	1(8.3%)	5(41.7%)	5(41.7%)	1(8.3%)	1.42	.71	.06
	No	20(5.2%)	153(39.4%)	131(33.8%)	84(21.6%)			
Fever	Yes	6(4.2%)	60(41.4%)	53(36.6%)	26(17.9%)	2.35	.50	.07

	No	15(5.9 %)	98(38.4 %)	83(32.5 %)	59(23.1 %)			
Headache	Yes	3(18.8 %)	5(31.3%)	6(37.5%)	2(12.5%)	5.33	.12	.13
	No	18(4.7 %)	153(39.8 %)	130(33.9 %)	83(21.6 %)			
Chest pain	Yes	2(66.7 %)	1(33.3%)	0(0.0%)	0(0.0%)	9.24	**.00**	.24
	No	19(4.8 %)	157(39.5 %)	136(34.3 %)	85(21.4 %)			
Nausea	Yes	2(8.3 %)	11(45.8 %)	8(33.3%)	3(12.5%)	1.64	.64	.06
	No	19(5.1 %)	147(39.1 %)	128(34 %)	82(21.8 %)			
Arthritis	Yes	3(3.9 %)	32(42.1 %)	21(27.6 %)	20(26.3 %)	2.71	.44	.08
	No	18(5.6 %)	126(38.9 %)	115(35.5 %)	65(20.1 %)			
Loss of sense of smell	Yes	0(0.0 %)	11(52.4 %)	8(38.1%)	2(9.5%)	3.63	.30	.09
	No	21(5.5 %)	147(38.8 %)	128(33.8 %)	83(21.9 %)			

Table 6 shows the chi square test results to find the association between side effects of COVID 19 vaccination and body mass index of individuals. Results revealed statistically significant relationship of body mass index with Hypotension ($\chi 2$ =8.954, p=0.030, V=0.150), numbness of limbs ($\chi 2$ =14.877, p=0.002, V= 0.193), chest pain ($\chi 2$ =23.416 p=0.008, V=0.242). The effect size for these variables lies in the small range (pallent 2010). Moreover, the table above also indicates that there was no significant relationship between diabetes with Allergic reaction, Myalgia, Pain at the site of injection, Hypertension, Fatigue, diarrhea, cough, Fever, Headache, Nausea, Arthritis, Loss of sense of smell/smell.

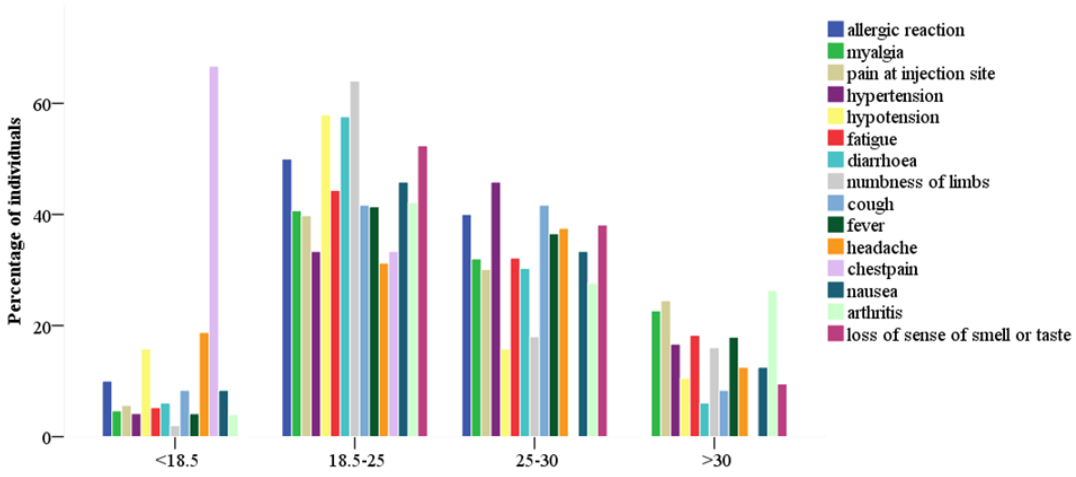

Figure 5 Side effects with different body mass indices

3.7. Glycemic Levels of Different Vaccines Between Diabetic And Non-Diabetic Groups

Table 7 Chi-square analysis of blood sugar levels in both groups

		Group		X^2	Sig.	V
		Diabetic	Non-diabetic			
Blood sugar level	<200mg/dl normal	145(44.9%)	178(55.1%)	17.514	**.000**	.209
	>200mg/dl high	55(71.4%)	22(28.6%)			

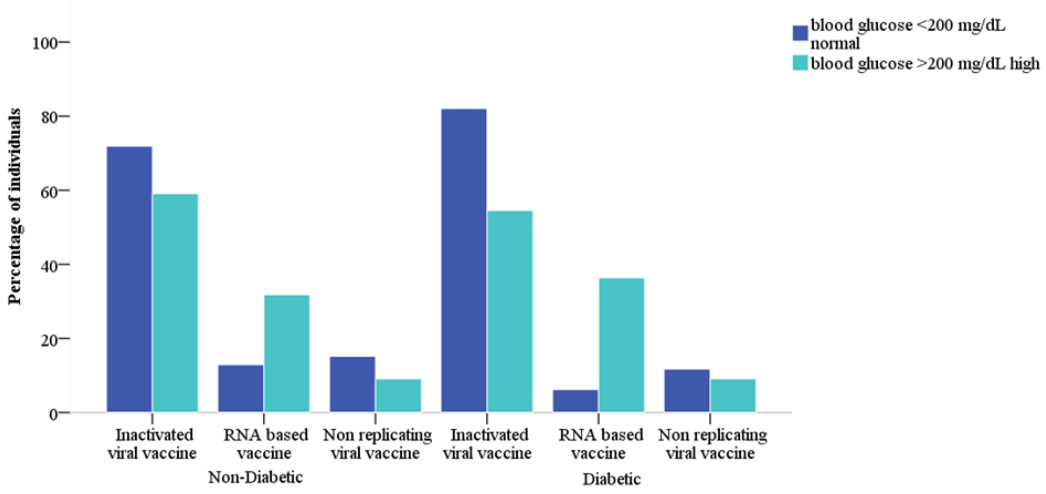

Figure 6 Blood sugar levels in both groups

3.8. Post Vaccine Biomarkers Level Vs Type Of Vaccine

Table 8 Chi-square analysis on type of vaccine with biomarkers

N=400	Type of vaccine						
		Inactivated viral vaccine	RNA based vaccine	Nonreplicating viral vaccine	$\chi 2$	p	V
LDL	<100mg/dL normal	209(72.1%)	42(14.5%)	399(13.4%)	.481	**0.81**	0.03
	>160mg/dL high	81(73.6%)	17(15.5%)	12(10.9%)			
TG	<150mg/dL normal	263(72.3%)	56(15.4%)	45(12.4%)	1.6141	**0.49**	0.06
	>200 mg/dL high	27(75.0%)	3(8.3%)	6(17.7%)			
Creatinine	0.6-1.1mg/dL normal	262(72.4%)	50(13.8%)	50(13.8%)	5.652	**0.05**	0.11

	>1.1mg/dL high	28(73.7%)	9(23.7%)	1(2.6%)			
TSH	.35-5.1uIU/mL normal	246(73.2%)	50(14.9%)	40(11.9%)	1.348	**0.50**	0.05
	>5.1uIU/mL high	44(68.8%)	9(14.9%)	11(17.2%)			
ALT	7-35U/L normal	260(72.0%)	54(15.0%)	47(13.0%)	.436	**0.89**	0.03
	>35U/L high	30(76.9%)	5(12.8%)	4(10.3%)			
CRP	<6.0 mg/L normal	264(72.1%)	57(15.6%)	45(12.3%)	2.761	**0.24**	0.08
	>6.0 mg/L high	26(76.5%)	2(5.9%)	6(17.6%)			
HBA1c	<6.5 % normal	139(70.6%)	30(15.2%)	28(14.2%)	.914	**0.63**	0.04
	>6.5 % Diabetic	151(74.4%)	29(14.3%)	23(11.3%)			

D Dimer	<500 mg/L normal	256(71.7 %)	54(15.1%)	47(13.2%)	1.054	**0.70**	0.05
	>500 mg/L high	34(79.1%)	5(11.6%)	4(9.3%)			

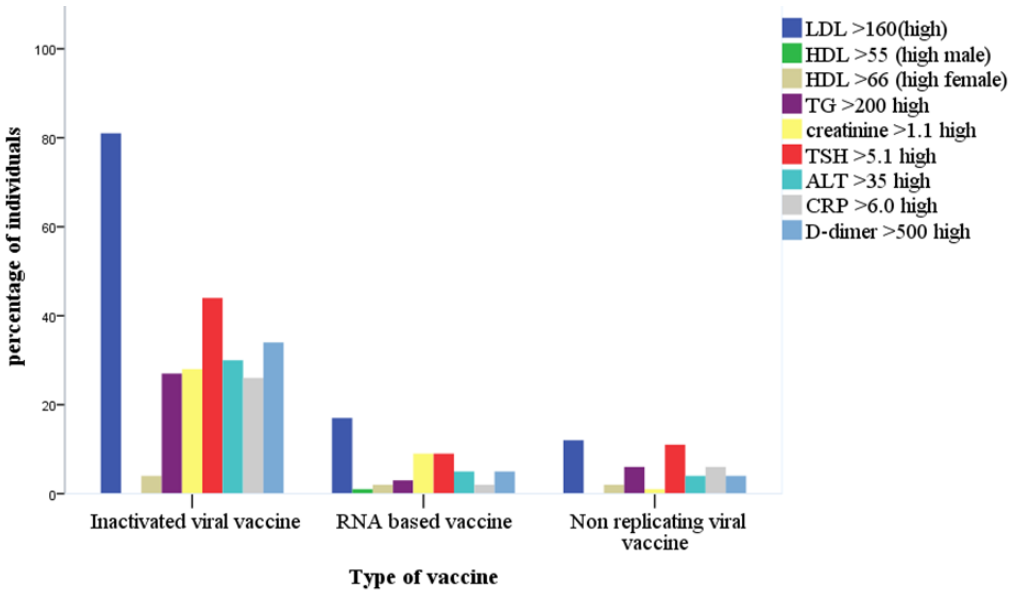

Figure 7 Levels of biomarkers in diabetic individuals with different vaccines

CHAPTER 4

DISCUSSION AND CONCLUSION

4. Discussion

The vaccination was the only treatment option for this pandemic at the beginning of the COVID-19 outbreak because there was no other medicinal approach. The inflammatory reaction is caused by vaccines, which also cause systemic and local problems. The post-vaccination effects vary depending on the host characteristics (age, gender, disease severity), the type of vaccine, and its composition. According to our hypothesis, after receiving COVID-19 vaccination, certain populations would probably have unfavorable reactions to the vaccine. As individuals with diabetes mellitus especially those with chronic complications are more vulnerable to the pandemic so all health care institutions have given precedence to vaccination in this group especially [15]. When comparing the age groups of 31–40 and 41–50 years, the acute adverse effects following immunizations are significantly higher in the younger age groups. The harmful effects of the mRNA vaccine have already been documented in individuals under the age of 33. This could be because of the study's available subjects fall within the 31–50 age range. In line with this, people with a body mass index of 18.5 to 25 kg/m2 were also noted to have hypotension [14].

All medical facilities have prioritized immunization in this category specifically because people with diabetes mellitus, especially those with chronic problems, are more susceptible to the pandemic [16]. According to the aforementioned findings, a total of 53.4% of diabetics and 46.6% of non-diabetics reported having an unfavorable reaction to the COVID-19 immunization. Following fever, weariness, headache, and pain at the injection site, adverse reactions at the injection site were most frequently reported by both inactivated and mRNA vaccine users. Our findings are consistent with

previously documented typical side effects of a different type of immunization, such as fever, pain at the injection site, arthritis, and myalgia.

Because high ALT levels have been associated with liver dysfunction, particularly when accompanied by jaundice, and ultimately autoimmune hepatitis, the levels of biomarkers can vary after immunization, which is worrisome [17]. A link between increased D-dimer and vaccine-induced thrombotic thrombocytopenia has been suggested in several cases where elevated D-dimer levels were discovered following immunization. To bolster the claim, more research is required on the connection between elevated creatinine levels and kidney disease.

4.1. Conclusion & Future Prospects

There are no significant differences between the post-vaccine effects in the two groups. The inactivated viral vaccine (Sinopharm, Sinovac) and non-replicating viral vaccination are safe, according to results (AstraZeneca, CanSino bio). After receiving an RNA-based vaccine, greater glycemic problems occur (Moderna, Pfizer). Concluded that diabetic patients could get the RNA-based vaccination (Moderna, Pfizer), but with precautions. The overall benefits of the COVID-19 vaccine outweigh any potential risks from side effects, especially for those with higher metabolic risk. Therefore, vaccination is advised for those with diabetes mellitus.

CHAPTER 5

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5. REFERENCES

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