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DERMATOLOGICAL MANIFESTATIONS ASSOCIATED WITH VACCINES AGAINST COVID-19: SYSTEMATIC REVIEW OF PUBLISHED CASES

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Abstract: Introduction: In 2021, population vaccination against COVID-19 began worldwide. The different vaccines used were associated with different dermatological manifestations in part of the population. **Objective**: To evaluate which were the most prevalent manifestations, their relationships with the type of vaccine, reaction time and epidemiological data (age and sex). **Methodology**: Systematic Literature Review, composed of reports or series of case reports selected from the databases: Google Scholar and PubMed, published between January 2021 and August 2022. The descriptors were: ‘’COVID-19”, ‘ ‘Dermatological”, ‘’Manifestations”, ‘’Vaccine”, with the filter ‘’Case Reports”. Statistical analysis was performed using the Microsoft Excel program. Articles belonging to other study modalities and which did not present reported cases were excluded. Continuous variables were presented as mean ± standard deviation and categorical data as percentages/absolute values. **Results**: 49 articles were selected, totaling 85 reported cases. The vaccines used were: Pfizer (54.11%), Covishield – Oxford Astrazeneca (19.99%), Moderna (18.82%), Coronavac (3.52%), Sinopharm – BBIBP-CorV (2.35%) and Covaxin (1.17%). The main dermatological manifestations observed were: herpes zoster (10.50%), ptiariasis rosea/ptiariasis rosea-like (9.41%), urticarial manifestations (9.41%), leukocytoclastic vasculitis (7.05%), rashes/ eczematous dermatitis (5.88%), perniosis/ chilblains (3.52%), ptiariasis rubra (2.35%), vitiligo (2.35%) and neutrophilic rash (2.35%). At Pfizer, the most recurrent manifestations were urticarial manifestations (15.21%), eruptions/eczematous dermatitis (10.86%) and herpes zoster (8.69%). At Covishield – Oxford Astrazeneca, the manifestations were Herpes Zoster (23.52%) and Ptiariasis Rosea/ Ptiariasis Rosea Like (17.64%). In Moderna, the manifestations were papules/chilblains

(18.75%), vitiligo (12.50%) and neutrophilic rash (12.50%). Among the 85 patients, there was only 1 death. **Final Considerations**: Considering that COVID-19 is a nosological entity still under discovery, the study of manifestations related to vaccines remains essential for the prevention of undesirable outcomes.
Key words: Coronavirus; COVID-19; Vaccine; Dermatological manifestations.

INTRODUCTION

In 2019, a new virus that causes mild to severe pneumonia, SARS-CoV-2, emerged in China, responsible for affecting more than 36.5 million people and causing the death of more than 1 million worldwide. The virus, which was widely spread by asymptomatic carriers, reached more than 200 countries and territories. The various vaccines were essential for preventing new outbreaks, controlling spread and preventing recurrence (SHARMA, Anshika; FARAOUK, Isra Ahmad; LAL, Sunil Kumar; 2021).

The vaccines cited in this work are Pfizer (RNA), Moderna (RNA), Oxford Astrazeneca (Non-Replicating Viral Vector), CoronaVac (Inactivated), Sinopharm BBIBP-CorV (inactivated) and Covaxin (Inactivated). RNA vaccines consist of a messenger RNA encoding an encapsulated viral antigen. They generate cellular and humoral responses and were the most used vaccines against COVID-19. Viral vector vaccines employ unrelated modified viruses as vectors to deliver antigen-encoding genes into cells to generate an immune response. These are vaccines that generate conditions that mimic an infection, which induce potent antibodies and T cells. Totally inactivated vaccines consist of viral culture particles inactivated by chemicals or radiation. These are vaccines with a more complete antigen repertoire, however, they generate weaker immune responses. All vaccine modalities can cause adverse effects, such as fatigue, fever, myalgia, headache. Normally, they are without major complications, however, there are also cases of more severe adverse effects, such as thrombosis, myocarditis or pericarditis, Guillian Barré Syndrome and allergic reactions. The objective of this work is to discuss the main dermatological manifestations associated with vaccines and whether they have a specific relationship with the type (RNA, Non-Replicating Viral Vector or Inactivated Virus) (CHI, Wei-Yu et al; 2022).

METHODOLOGY

The work is a Systematic Literature Review, composed of reports or series of case reports selected from the databases: Google Scholar and PubMed, published between January 2021 and August 2022. The descriptors were: ‘’COVID-19”, ‘’Dermatological”, ‘’Manifestations”, ‘’Vaccine”, with the ‘’Case Reports” filter. Statistical analysis was performed using the Microsoft Excel program. Articles belonging to other study modalities and which did not present reported cases were excluded. After selecting articles in Portuguese and English, the data were organized in a table, divided into categories: authors, sex, age, vaccine received, at which dose the manifestation occurred, how many days after application and clinical manifestation. Continuous variables were presented as mean ± standard deviation and categorical data as percentages/absolute values.

RESULTS

49 articles were selected, totaling 85 reported cases. Of the patients, 54.11% received the Pfizer vaccine, 18.82% received Moderna, 15.29% received Oxford Astrazeneca, 4.7% received Covishield, 3.52% received Coronavac, 2.35% received

Sinopharm (BBIBP-CorV) and 1.17% received Covaxin. In general, the age of individuals who presented post-vaccine dermatological manifestations was 51.84 ± 17.57 years and 56.4% were male. The reaction occurred after the 1st dose in 57.64% of cases, 5.41 ± 5.05 days later. In relation to Pfizer, the age was 51.80 ± 18.09 years and 58.69% were male. The reaction occurred after the 2nd dose in 52.17% of cases, in 5.62 ± 5.56 days. In relation to Moderna, the age was 62.18 ± 12.45 years, with 62.5% female. The reaction occurred after the 1st dose in 68.75% of patients, 4.93 ± 4.46 days later. In the Astrazeneca vaccine, the age was 46.29 ± 14.56 years, and 70.5% were male. The reaction occurred after the 1st dose in 70.5% of cases, 5.45 ± 4.45 days later. Among the main dermatological manifestations observed in general in all vaccines, there were herpes zoster (10.50%), ptiariasis rosea/ptyariasis rosea-like (9.41%), urticarial manifestations (9.41%), vasculitis leukocytoclastic rash (7.05%), eczematous rash/dermatitis (5.88%), perniosis/chilblains (3.52%), ptiariasis rubra (2.35%), vitiligo (2.35%), and neutrophilic rash (2.35%). At Pfizer, the most recurrent manifestations were urticarial manifestations (15.21%), eruptions/eczematous dermatitis (10.86%) and herpes zoster (8.69%). In Moderna, the manifestations were papules/chilblains (18.75%), vitiligo (12.50%) and neutrophilic rash (12.50%). In Astrazeneca, the main ones were Herpes Zoster (23.52%) and Ptiariasis Rosea/Ptiariasis Rosea Like (17.64%). Among the 85 patients, there was only 1 death.

DISCUSSION

Vaccines have different adverse effects, which is why it is important for professionals to recognize their signs and symptoms. In general, the symptom that was most present was erythema in the region where the vaccine was administered, and the most frequent and important clinical condition is Herpes Zoster (HZ), which requires specific care. Men aged close to 50 years old, which is in accordance with the literature, since the chances of HZ reactivation are greater with age, and who received doses of the Astrazeneca vaccine were those most affected by Herpes Zoster. The Varicella Zoster virus is a neurotropic virus that remains dormant in the dorsal root ganglia or cranial nerves. Situations of immunosuppression or trauma can lead to its reactivation, which can be observed in some vaccines (COVID-19, Hepatitis A, rabies) (EID, Edward, 2021). Among other clinical manifestations, the origins are diverse: immediate or delayed hypersensitivity (erythema, rigidity); autoimmune reactions (Lupus erythematosus, bullous pemphigoid, leukocytoclastic vasculitis, vitiligo); functional angiopathies (chilblains) and reactivation of other viral conditions. It is important to recognize each clinical condition for appropriate treatment, as well as identifying which vaccine produces effects most frequently (GAMBICHLER, et al; 2022).

AUTHORS	SEX	AGE	WHICH VACCINE	WHAT DOSE	DAYS LATER	MANIFESTATION
VAN DAM, et al.	F	29	PFIZER	1	15	HERPES ZOSTER
VAN DAM, et al.	M	34	PFIZER	1	13	HERPES ZOSTER
KONG, et al.	M	66	MODERN	two	1	BULLOUS ERUPTION
PEDRAZINI, MC; DA SILVA, MH	M	53	ASTRAZENECA	two	15	PTIARIASIS ROSEA LIKE
SIRUFO, et al.	F	76	ASTRAZENECA	1	7	PURPLE BY HENOCH-SCHONLEIN
ALSHAMMARI, et al.	M	78	PFIZER	two	1	BULLOUS PEMPHIGOID
DASH, et al.	M	60	ASTRAZENECA	1	3	SYNDROME BY STEVENS-JOHNSON
YATSUZUKA, et al.	M	65	PFIZER	two	12	ERYTHEMATOUS PLAQUES AND PUSTULES
FATA, et al.	F	33	PFIZER	1	1	MACULOPAPULAR PATTERN UNUSUAL
CRIADO, et al	M	31	ASTRAZENECA	1	10	PTYARIASIS RUBRA PILARS TYPE 1
CRIADO, et al	M	42	ASTRAZENECA	two	8	PTYARIASIS RUBRA PILARS TYPE 1
MERRIL, et al.	M	50	MODERN	1	1	NEUTROPHILIC ERUPTION FACIAL PUSTULARY
MERRIL, et al.	M	80	MODERN	two	1	NEUTROPHILIC ERUPTION FACIAL PUSTULARY
AWADH, el al	M	18	PFIZER	1	two	PAPULOVESICULAR ERUPTION GENERALIZED
MEHTA, et al.	F	25	ASTRAZENECA	1	7	ERYTHEMATOUS NODULES AND PAINFUL
MEHTA, et al.	M	55	ASTRAZENECA	1	3	HERPES ZOSTER
MEHTA, et al.	M	24	ASTRAZENECA	1	1	PINK PTYRIASIS
BORG, et al.	M	38	PFIZER	1	two	ERYTHEMA MULTIFORME BULLOSUS
MOHTA, et al.	M	34	ASTRAZENECA	1	7	HERPES ZOSTER
MOHTA, et al.	M	57	ASTRAZENECA	1	5	HERPES ZOSTER
MOHTA, et al.	M	38	ASTRAZENECA	1	4	HERPES ZOSTER
BASSI, et al.	F	52	MODERN	1	7	SIMILAR INJURIES FREEZING
OSKAY, T; ISIK, M.	M	77	CORONAVAC	3	14	VASCULITIS LEUKOCYTOCLASTIC
JEDLOWSKI, PM; JEDLOWSKI, MF;	M	30	PFIZER	1	two	MORBILIFORME RASH
GRISS, et al.	F	77	MODERN	1	14	SKIN INFARCTS MULTI-LOCATED
KAR, et al.	F	46	COVAXIN	1	5	PURPURIC PAPULES
KRAJEWSKI, et al.	M	46	PFIZER	two	1	PSORIASIFORM LESIONS
YOUNG, et al.	M	68	PFIZER	1	3	BULLOUS ERYTHEMA AND ORAL ULCER
HOLMES, et al.	F	68	MODERN	1	two	ANGIOEDEMA AND URTICARIFORM RASH
HOLMES, et al.	F	86	PFIZER	two	5	URTICARIFORM VASCULITIS
HOLMES, et al.	F	48	MODERN	1	10	CHIBLAINS-LIKE PAPULES

HOLMES, et al.	F	33	MODERN	two	1	MORBILIFORME ERUPTION WITH PLATES
HOLMES, et al.	M	37	PFIZER	1	7	ECZEMATOUS DERMATITIS
LEE, et al.	M	77	MODERN	1	two	HERPES ZOSTER
LEE, et al.	M	65	PFIZER	two	14	HERPES ZOSTER
MAZZATENTA, et al.	F	44	PFIZER	two	21	PURPLES
MAZZATENTA, et al.	M	63	PFIZER	two	21	PURPLES
MAZZATENTA, et al.	F	67	PFIZER	1	10	PURPUES AND CRUSHES
PICONE, et al.	M	60	MODERN	1	7	ERYTHEMATOUS RASH
PICONE, et al.	F	62	MODERN	1	7	ERYTHEMATOUS RASH
COTO-SEGURA, et al.	M	86	PFIZER	two	17	URTICARIFORM PLATES AND ERYTHEMATOUS
COTO-SEGURA, et al.	M	85	PFIZER	two	8	URTICARIFORM PLATES AND ERYTHEMATOUS
COTO-SEGURA, et al.	M	84	PFIZER	two	7	URTICARIFORM PLATES AND ERYTHEMATOUS
COTO-SEGURA, et al.	M	71	PFIZER	two	3	VESICLES
BENCHARATTANAPHAKHI, R,; RERKNIMITR, P.	F	23	CORONAVAC	1	1.5	VASCULITIS LEUKOCYTOCLASTIC
BENCHARATTANAPHAKHI, R,; RERKNIMITR, P.	F	26	CORONAVAC	1	0.16	VASCULITIS LEUKOCYTOCLASTIC
BELINA, et al.	F	42	PFIZER	two	3	LICHEN STRIATUS
SANDHU, et al.	F	55	ASTRAZENECA	1	5	VASCULITIS LEUKOCYTOCLASTIC
SANDHU, et al.	M	48	ASTRAZENECA	two	two	VASCULITIS LEUKOCYTOCLASTIC
HECK, et al.	M	48	ASTRAZENECA	1	0.16	PURPLE
HUANG, et al.	M	19	BBIBP-CorV	1	two	PTYRIASIS ROSEA
HUANG, et al.	M	51	BBIBP-CorV	two	7	PTYRIASIS ROSEA
LOPEZ, et al.	M	58	PFIZER	two	4	PSORIASIFORM DERMATITIS AND SPONGIOTIC
COHEN, et al.	M	66	PFIZER	1	7	PYTHRIASIS ROSEA
MILITELLO, et al.	F	67	MODERN	1	14	VITILIGO
KHA, et al.	F	70	MODERN	1	two	PERNIOSIS (CHILBAINS)
KHA, et al.	F	70	MODERN	two	3	PERNIOSIS
ALHAMMAD, et al.	F	28	ASTRAZENECA	two	0.5	MORBILIFORME RASH
BUCKLEY, et al.	F	23	PFIZER	1	7	PYTHRIASIS ERUPTIONS ROSEA-LIKE
LEERUNYAKUL, et al.	F	52	ASTRAZENECA	1	14	PYTHRIASIS ERUPTIONS ROSEA-LIKE
SECHI, et al.	F	24	PFIZER	two	two	PERIFLEXURAL RASH UNILATERAL
ATIYAT R, et al.	M	36	PFIZER	two	7	HERPES ZOSTER
KAMINETSKY J.; RUDIKOFF, D.	M	61	MODERN	two	3	VITILIGO
COHEN SR et al	M	46	PFIZER	two	two	PSORIASIS, ARTHRITIS PSORIATIC
HILTUN J.S, et al	F	56	PFIZER	two	two	LICHEN PLANU
LEASURE, et al.	M	43	PFIZER	1	3	ECZEMATOUS ERUPTIONS GENERALIZED

LEASURE, et al.	M	43	PFIZER	two	14	ECZEMATOUS ERUPTIONS GENERALIZED
LEASURE, et al.	F	51	PFIZER	1	4	ECZEMATOUS ERUPTIONS GENERALIZED
LEASURE, et al.	F	51	PFIZER	two	4	ECZEMATOUS ERUPTIONS GENERALIZED
CORBEDDU, el al.	F	67	PFIZER	1	1	PLATE ERYTHEMATO-EDEMATOSA
CORBEDDU, el al.	F	67	PFIZER	1	1	PLATE ERYTHEMATO-EDEMATOSA
CORBEDDU, el al.	F	61	PFIZER	two	two	ERYTHEMA AND EDEMA ON THE BACK OF THE FOOT
CORBEDDU, el al.	F	55	PFIZER	1	8	FACIAL ERYTHEMA AND ITCHING
CORBEDDU, el al.	F	59	PFIZER	two	3	ERYTHEMATOUS RASH DIFFUSE
CORBEDDU, el al.	F	62	PFIZER	1	0.04	PLATE ERYTHEMATO-EDEMATOSA
CORBEDDU, el al.	F	38	PFIZER	1	0.04	ERYTHEMA OF BOTH LEGS
CORBEDDU, el al.	M	56	PFIZER	1	0.04	URTICARIA AT THE INJECTION SITE
CORBEDDU, el al.	F	56	PFIZER	two	0.2	ERYTHEMATOUS RASH DIFFUSE OF THE TRUNK
CORBEDDU, el al.	M	29	PFIZER	1	7	ERYTHEMA AND SWELLING LEFT CHEST
CORBEDDU, el al.	M	36	PFIZER	two	two	ERYTHEMATOUS RASH DIFFUSE OF THE TRUNK
CORBEDDU, el al.	M	32	PFIZER	1	two	URTICARIFORM ERUPTION ,ATOPIC DERMATITIS CRISIS
LIM, PN; WYLIE, G.	M	61	ASTRAZENECA	two	1	FLEXURAL RASH AND INTERTRIGINOUS
JOSEPH, K.A; CHONG, B.F.	F	54	MODERN	1	4	LUPUS ERYTHEMATOSUS SUBACUTE CUTANEOUS
LOPES, et al.	M	64	PFIZER	two	3	ACRAL LEG TYPE INJURIES
CARBALLIDO VÁZQUEZ, AM; MORGADO, B.	M	35	PFIZER	1		PTYRIASIS ROSEA LIKE

Table 01: Clinical-demographic relationships of the main dermatological manifestations associated with vaccines against COVID-19.

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