

## ASSOCIATION BETWEEN MEDICATION USE AND BULLOUS PEMPHIGOID: A TEN-YEAR SYSTEMATIC REVIEW

<sup>1\*</sup>Ronauli Agnes Marpaung, <sup>1</sup>Fina Retnawati Sihombing

<sup>1</sup>Aeramo Regional General Hospital, Nagekeo Regency, Indonesia

**Correspondence Author:**  
[ronauliagnes@gmail.com](mailto:ronauliagnes@gmail.com)

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### ABSTRACT

**Background:** Bullous pemphigoid is an autoimmune subepithelial disease. It was associated with autoantibodies targeting hemidesmosome protein BPAG1 and BPAG2. The incidence of bullous pemphigoid has increased 1.9-4.3 times in the past two decades, possibly due to increased life expectancy, medication use, and improved diagnostic methods. Trigger factors of BP included drugs, physical factors, radiotherapy, trauma, and thermal exposure.

**The aim:** This study aims to determine association between medication use and bullous pemphigoid.

**Methods:** By comparing itself to the standards set by the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, this study was able to show that it met all of the requirements. So, the experts were able to make sure that the study was as up-to-date as it was possible to be. For this search approach, publications that came out between 2014 and 2024 were taken into account. Several different online reference sources, like Pubmed and ScienceDirect, were used to do this. It was decided not to take into account review pieces, works that had already been published, or works that were only half done.

**Results:** In the PubMed database, the results of our search brought up 1,662 articles, whereas the results of our search on ScienceDirect brought up 1,143 articles. The results of the search conducted by title screening yielded a total of 13 articles for PubMed and 32 articles for ScienceDirect. We compiled a total of 26 papers, 8 of which came from PubMed and 18 of which came from ScienceDirect. We excluded 2 review articles, 1 duplicate article, 3 non-full text articles, and 3 articles having insufficient outcomes. In the end, we included seventeen research that met the criteria.

**Conclusion:** Our study suggests that dipeptidyl peptidase-4 inhibitors and aldosterone antagonists are associated with BP. Other medications, such as immunomodulatory agents, anticonvulsants, tyrosine kinase inhibitors, antibiotics, anticoagulants, diuretics, and mRNA COVID-19 vaccine, may be associated with BP. Regarding these results, clinicians should pay close attention to prescribing the medicine to their patients.

**Keywords:** Medication, drugs, bullous pemphigoid, DIBP

## INTRODUCTION

Bullous pemphigoid is an autoimmune subepithelial disease characterized by generalized pruritus urticaria and tight blisters caused by subepithelial detachment and inflammation with an abundance of eosinophils.<sup>1,2</sup> Older people were frequently afflicted with bullous pemphigoid. Bullous pemphigoid is influenced by age and genetics.<sup>3</sup> The pathogenesis is dysregulated by autoantibodies targeting two main structural proteins of the dermal-epidermal junction, hemidesmosome protein BP antigen 1 (BPAG1 or BP230 antigen) and BPAG2 (BP180 antigen).<sup>1,2</sup> The basement membrane zone is degraded, and neutrophil chemotaxis results from this reaction.<sup>2</sup> Diagnosis of bullous pemphigoid was based on clinical features, histological findings, and immunopathological studies, including direct and indirect immunofluorescence microscopy, and enzyme-linked immunosorbent assays (ELISA) for BP180 and BP230.<sup>4</sup> First-line treatment of bullous pemphigoid is topical and systemic corticosteroids. The therapy depends on comorbidities and the extent of the disease.<sup>5,6</sup>

Bullous pemphigoid incidence has risen 1.9-4.3 times in the past 2 decades, possibly due to increased life expectancy, medication use, awareness of atypical variants, and improved diagnostic methods.<sup>1</sup> Bullous pemphigoid has an association with specific trigger factors, such as medication or drugs, physical factors, radiotherapy, trauma, thermal, and others. Many studies suggest an association between medication use and bullous pemphigoid. Drugs allegedly associated with bullous pemphigoid were systemic therapy, such as antibiotics (penicillins and quinolones groups), beta-blockers, NSAIDs (aspirin, celecoxib), diuretics (furosemide), anti-tumor necrosis factor (TNF)- $\alpha$ , dipeptidyl peptidase 4 inhibitors (DPP-4i) - vildagliptin, sitagliptin; and immune checkpoint inhibitors targeting programmed cell death receptor 1 (PD-1) and its ligand (PD-L1).<sup>1,6,7</sup> Older age, neurological disorders (dementia, including Alzheimer's disease and other types of dementia, and stroke), and elevated blood levels of anti-BP180 NC16A IgG are risk factors associated with increased mortality in bullous pemphigoid.<sup>2</sup> The purpose of this study is to determine association between medication use and bullous pemphigoid.

## METHODS

### Protocol

By following the rules provided by Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, the author of this study made certain that it was up to par with the requirements. This is done to ensure that the conclusions drawn from the inquiry are accurate.

### Criteria for Eligibility

For the purpose of this literature review, we investigate the association between medication use and bullous pemphigoid. It is possible to accomplish this by researching or investigating the occurrence of BP and the association of medications or drugs with bullous pemphigoid. As the primary purpose of this piece of writing, demonstrating the relevance of the difficulties that have been identified will take place throughout its entirety.

In order for researchers to take part in the study, they needed to fulfil the following requirements: 1) The paper needs to be written in English, and it needs to determine the association between medication use and bullous pemphigoid. In order for the manuscript to be considered for publication, it needs to meet both of these requirements. 2) The studied papers include several that were published after 2014, but before the time period that this systematic review deems to be relevant. Examples of studies that are not permitted include editorials, submissions that do not have a DOI, review articles that have already been published, and entries that are essentially identical to journal papers that have already been published.

### Search Strategy

We used "medication"; "drugs"; "bullous pemphigoid"; and "DIBP" as keywords. The search for studies to be included in the systematic review was carried out from February, 18th 2024 using the PubMed and ScienceDirect databases by inputting the words: "medic"[All Fields] OR "medical"[All Fields] OR "medicalization"[MeSH Terms] OR "medicalization"[All Fields] OR "medicalizations"[All Fields] OR "medicalize"[All Fields] OR "medicalized"[All Fields] OR "medicalizes"[All Fields] OR "medicalizing"[All Fields] OR "medically"[All Fields] OR "medicals"[All Fields] OR "medicated"[All Fields] OR "medication s"[All Fields] OR "medics"[All Fields] OR "pharmaceutical preparations"[MeSH Terms] OR "pharmaceutical"[All Fields] AND "preparations"[All Fields] OR "pharmaceutical preparations"[All Fields] OR "medication"[All Fields] OR "medications"[All Fields] OR "drug s"[All Fields] OR "pharmaceutical preparations"[MeSH Terms] OR ("pharmaceutical"[All Fields] AND "preparations"[All Fields] OR "pharmaceutical preparations"[All Fields] OR "drugs"[All Fields] AND "pemphigoid, bullous"[MeSH Terms] OR "pemphigoid"[All Fields] AND "bullous"[All Fields] OR "bullous pemphigoid"[All Fields] OR "bullous"[All Fields] AND "pemphigoid"[All Fields] OR "DIBP"[All Fields] AND (y\_10[Filter]) AND (english[Filter]) used in searching the literature.

### Data retrieval

After reading the abstract and the title of each study, the writers performed an examination to determine whether or not the study satisfied the inclusion criteria. The writers then decided which previous research they wanted to utilise as sources

for their article and selected those studies. After looking at a number of different research, which all seemed to point to the same trend, this conclusion was drawn. All submissions need to be written in English and can't have been seen anywhere else.

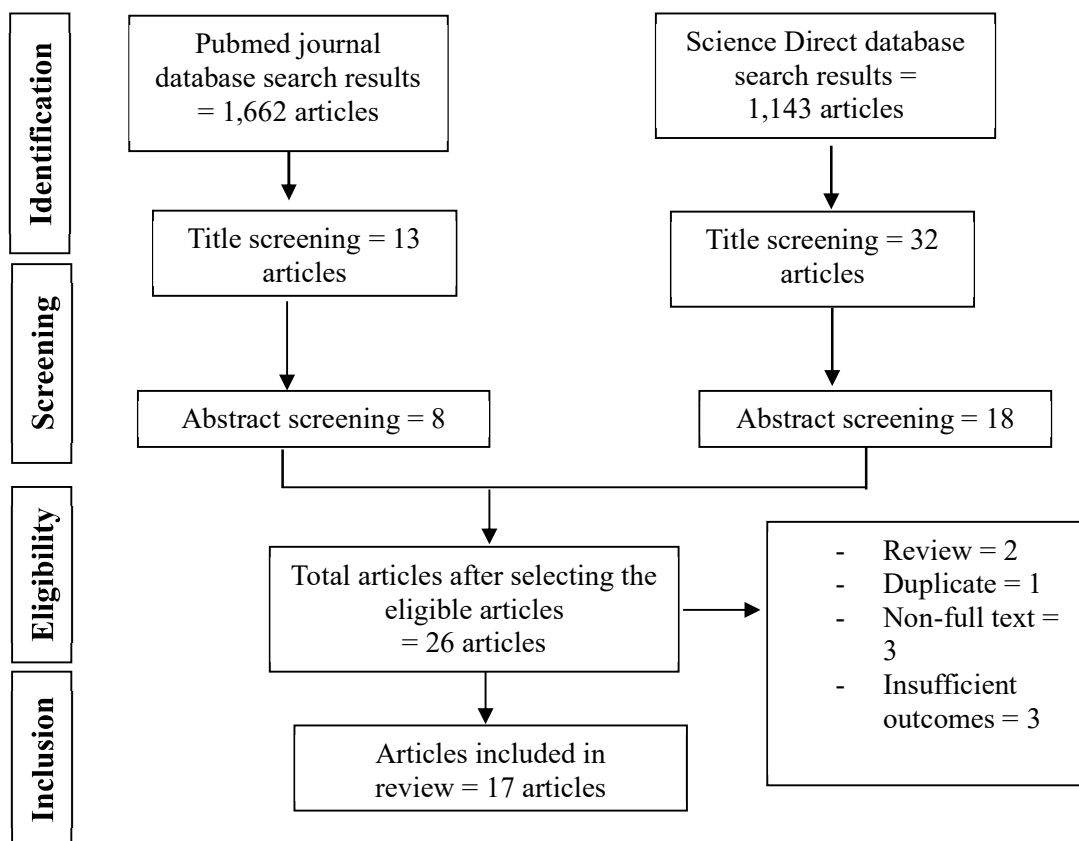


Figure 1. Article search flowchart

Only those papers that were able to satisfy all of the inclusion criteria were taken into consideration for the systematic review. This reduces the number of results to only those that are pertinent to the search. We do not take into consideration the conclusions of any study that does not satisfy our requirements. After this, the findings of the research will be analysed in great detail. The following pieces of information were uncovered as a result of the inquiry that was carried out for the purpose of this study: names, authors, publication dates, location, study activities, and parameters.

**Quality Assessment and Data Synthesis**

Each author did their own study on the research that was included in the publication's title and abstract before deciding on which publications to explore further. The next step will be to evaluate all of the articles that are suitable for inclusion in the review because they match the criteria set forth for that purpose in the review. After that, we'll determine which articles to include in the review depending on the findings that we've uncovered. This criteria is utilised in the process of selecting papers for further assessment to simplify the process as much as feasible when selecting papers to evaluate. Which earlier investigations were carried out, and what elements of those studies made it appropriate to include them in the review, are being discussed here.

**RESULT**

In the PubMed database, the results of our search brought up 1,662 articles, whereas the results of our search on ScienceDirect brought up 1,143 articles. The results of the search conducted by title screening yielded a total of 13 articles for PubMed and 32 articles for ScienceDirect. We compiled a total of 26 papers, 8 of which came from PubMed and 18 of which came from ScienceDirect. We excluded 2 review articles, 1 duplicate article, 3 non-full text articles, and 3 articles having insufficient outcomes. In the end, we included seventeen research that met the criteria.

**Table 1. The literature included in this study**

Author	Origin	Method	Sample Size	Result
Alshammari, 2022 <sup>8</sup>	Saudi Arabia	Case report	1 patient	This case report suggests that the mRNA-Covid-19 (Pfizer) vaccine may be the cause of bullous pemphigoid.
Arslan, 2023 <sup>9</sup>	Turkey	Case report	1 patient	This case report is the initial instance of a bullous medication reaction linked to teriflunomide. During the first three months of DMT, teriflunomide-induced bullous pemphigoid was identified. After stopping teriflunomide and receiving systemic steroid therapy, it has entirely recovered.
Benzaquen, 2018 <sup>10</sup>	Europe	Case control	61 patients	This case-control study results validate that DPP4is are linked to a higher risk of blood pressure development in diabetic patients. Therefore, in high-risk individuals, such as males and those 80 years of age or older, the prescription of a DPP4i, particularly vildagliptin, may possibly be limited or avoided.
Flamm, 2017 <sup>11</sup>	USA	Case report	1 patient	With no prior rashes or pharmaceutical responses, this case is the first to document a direct link between the onset of gabapentin and bullous pemphigoid. In addition to supporting the link between gabapentin and bullous pemphigoid, the patient's symptoms disappeared after stopping the medication in less than a month.
Guern, 2015 <sup>12</sup>	France	Case report	1 patient	This case report is the first instance of bullous pemphigoid treated with ustekinumab.
Guo, 2020 <sup>13</sup>	Taiwan	Retrospective study	14,187 patients	Dipeptidyl peptidase-4 inhibitors have been linked to a higher chance of BP development in T2DM patients. Individuals with dementia who were also taking spironolactone had an increased risk.
Hasson, 2019 <sup>14</sup>	USA	Case report	1 patient	This study report nintedanib induced Bullous pemphigoid.

Iguchi, 2023 <sup>15</sup>	Japan	Case report	1 patient	According to this case report, oral mucosal sores may be a presenting feature of DPP-4i-associated BP. For this reason, when treating patients with oral blistering illnesses, doctors should carefully review their drug histories and medical histories.
Kridin, 2018 <sup>16</sup>	Israel	Case control	82 patients	The use of DPP-4 inhibitor overall and vildagliptin and linagliptin individually was found to increase the risk for BP significantly. Discontinuation of treatment with DPP-4 inhibitors was followed by better clinical outcomes, suggesting that such discontinuation should be considered when the diagnosis of BP is established. The increased exposure to these agents in recent years may account for the increasing incidence of BP in our region.
Liang, 2021 <sup>17</sup>	Canada	Case report	1 patient	This is the first case of rivaroxaban-associated BP linked to immunofluorescence confirmation that has been documented. Patients who have suspected drug-associated BP should promptly stop using rivaroxaban and switch to another anticoagulant.
Qiu, 2020 <sup>18</sup>	USA	Case report	1 patient	In this case report, patient presents with a bullous pemphigoid that mimics toxic epidermal necrolysis, which was caused by pembrolizumab.
Sanchez, 2023 <sup>19</sup>	USA	Case report	1 patient	This case study revealed that the patient's development of BP was largely caused by phototoxicity induced by doxycycline.
Santaliz-Ruiz, 2022 <sup>20</sup>	Puerto Rico	Case report	1 patient	An example of DIBP secondary to levetiracetam was reported in this study involving a young adult female.
Sun, 2019 <sup>21</sup>	USA	Case report	2 patients	Two individuals with BP were described in this case study following pembrolizumab medication.

Wu, 2021 <sup>22</sup>	Taiwan	Cohort	124,619 patients	The findings of this study suggested that DPP4is were linked to a 2.2-fold increase in BP risk, with the risk being highest in individuals using DPP4is and insulin concurrently.
Wurtz, 2022 <sup>23</sup>	Nebraska	Case report	1 patient	Torsemide should be taken into consideration as a possible culprit when the history, examination, and histology are in line with DABP, as it is possible that it could cause BP by processes similar to those of furosemide.
Yanai, 2023 <sup>24</sup>	Japan	Case report	1 patient	In this investigation, a case of DPP-4i-BP with oral symptoms was reported.

### Occurrence of Bullous Pemphigoid in Association with Medication Use

Thirteen case reports<sup>8,9,11,12,14,15,17-21,23,24</sup> were reporting the occurrence of bullous pemphigoid after medication use. The drug most frequently reported was dipeptidyl peptidase-4 inhibitors (vildagliptin, sitagliptin, linagliptin) while other medications reported include immunomodulatory agents (teriflunomide, ustekinumab, pembrolizumab), anticonvulsants (gabapentin, levetiracetam), tyrosine kinase inhibitor (nintedanib), antibiotics (doxycycline), anticoagulant (rivaroxaban), diuretics (torsemide), and mRNA Covid-19 vaccine (Pfizer). In addition, aldosterone antagonists were also reported in other studies.<sup>13</sup>

Two retrospective cohort studies showed that the incidence rate was higher in DPP4i group than in control group.<sup>13,22</sup> Guo, et al. (2020)<sup>13</sup> showed that the DPP4i group experienced a higher incidence rate of BP (1.41 vs. 0.59 per 1000 person-years; adjusted HR 2.14, 95% CI = 1.02–4.50) compared to the control group. Wu, et al. (2021)<sup>22</sup> showed that with an incidence rate ratio of 1.61 (95% CI: 1.04–2.48), the incidence rates of BP in the DPP4i-treated and non-DPP4i-treated groups were 11.0 and 6.9 per 100,000 person-years, respectively.

Two case-control studies showed that DPP4is were used more frequently in case patients with BP.<sup>10,16</sup> Kridin, et al. (2018)<sup>16</sup> showed that at enrollment, 71 (21.6%) control individuals had received treatment with DPP-4 inhibitor, whereas thirty-six (44%) case-patients with BP had received it at the beginning (P <.001). Vildagliptin was the most often prescribed DPP-4 inhibitor among cases, having been given to 24 case-patients (29%) and 14 control participants (4.3%) (P <.001). The prevalence of linagliptin was higher in case patients (n = 9; 11%) compared to controls (n = 6; 4.7%; P =.03). Remarkably, compared to controls (n = 51; 15.5%), case patients (n = 6; 7%) used sitagliptin less frequently (P =.047). Benzaquen, et al. (2018)<sup>10</sup> showed that statistical analysis revealed that DPP4is were utilized significantly more often (P <.001) in case patients with BP (45.9%) than in controls (18%). Between case-patients (23%) and controls (4.1%), vildagliptin was used more frequently.

### Association of Medication Use and Bullous Pemphigoid

Kridin, et al. (2018)<sup>16</sup> showed that the consumption of DPP-4 inhibitors was found to be statistically significantly associated with the development of BP (OR, 2.83; 95% CI, 1.70-4.71). Patients under 70 years old had the highest correlation (OR, 5.59; 95% CI, 1.73-18.01). In comparison to female patients (OR, 1.88; 95% CI, 0.92-3.86), the connection was stronger in male patients (OR, 4.46; 95% CI, 2.11-9.40). The most significant association between vildagliptin use and BP was shown (OR, 9.28; 95% CI, 4.54-18.99). The development of BP had a significant association with linagliptin usage (OR, 6.61; 95% CI, 2.28-19.17). There was a lack of association found between the onset of BP and sitagliptin treatment.

Benzaquen, et al. (2018)<sup>10</sup> showed that in diabetic patients, the univariate analysis of the association between DPP4i usage and BP produced an OR of 3.45 (95% CI, 1.76-6.77; P <.001). Following multivariate analysis and correction for potential confounding variables related to BP onset and DPP4i use, the OR was 2.64 (95% CI, 1.19-5.85; P =.02). Vildagliptin showed a greater association with DPP4i use, with an adjusted OR of 3.57 (95% CI, 1.07-11.84; P =.04) and a crude OR of 7.23 (95% CI, 2.44-21.40; P =.001). Males had a greater effect of a DPP4i on BP onset (adjusted OR, 4.36; 95% CI, 1.38-13.83; P =.01) than females did (adjusted OR, 1.64; 95% CI, 0.53-5.11; P =.39), according to sex-stratified analysis. Patients 80 years of age or older showed a more significant association, with an adjusted OR of 5.31 (95% CI, 1.60-17.62; P =.006) in age group stratified analyses.

Guo, et al. (2020)<sup>13</sup> showed that regarding drugs or medications, patients on metformin had a lower crude-associated risk (adjusted HR 0.38, 95% CI = 0.18–0.79), but those on insulin and spironolactone had greater crude-associated risks (HR 2.46, 95% CI = 1.13–5.35) and 5.50, 95% CI = 2.38–12.72). In individuals on spironolactone, the increased risk persisted even after controlling for covariates (adjusted HR 3.06, 95% CI = 1.25–7.51).

Wu, et al. (2021)<sup>22</sup> showed that an elevated risk of BP was linked to age (HR: 1.06), renal disease (HR: 2.32), and metformin users (HR: 1.93). DPP4i and insulin did not significantly interact (HR: 0.65, 95% CI: 0.29–1.50, P = 0.31). In the DPP4i-treated group, the total risk of BP was 1.75 times higher (95%CI: 1.14–2.67).

## DISCUSSION

Bullous pemphigoid had often been linked to the assumption of systemic treatments. When patients recently switch drugs, they should be closely monitored for drug-associated bullous pemphigoid, particularly if those medications are strongly linked to bullous pemphigoid. The medications include DPP-4i, antibiotics, NSAIDs, beta-blockers, diuretics, TNF- $\alpha$ , and immune checkpoint inhibitors targeting programmed cell death receptor 1 (PD-1) and its ligand (PD-L1).<sup>6,25</sup> The main components of bullous pemphigoid pathophysiology are immunologic and inflammatory.<sup>5</sup> Bullous pemphigoid autoantibodies primarily target BP180 and BP230, hemidesmosomal proteins of dermo-epidermal junction. Based on Moro et al, previous use of DPP-4i has the highest risk of bullous pemphigoid event. It was understood that DPP-4 functions as a receptor for cell surface plasminogen, activating plasminogen and causing it to produce plasmin, a significant serine protease that cleaves BP180's NC16A domain. The proper cleavage of BP180 may be altered due to DPP-4i's suppression of plasmin, changing the antigenicity and function of the protein. Moreover, DPP-4 was expressed by keratinocytes, endothelial cells, and T cells; its suppression may boost the action of proinflammatory cytokines such as eotaxin, causing cutaneous eosinophil activation and bullous formation to occur.<sup>6</sup> In Varpuluoma et al study, found that DPP-4i had a significant association with an increased risk of bullous pemphigoid. The study found that using vildagliptin can increase the risk of bullous pemphigoid to ten times. The other finding of this study is women were more likely to get bullous pemphigoid than men.<sup>26</sup> According to Liu et al study, using DPP-4i was significantly associated with bullous pemphigoid.<sup>1</sup> This finding is consistent with our finding that suggests the use of DPP-4i is significantly associated with bullous pemphigoid.

In our study, many immunomodulatory agents, such as teriflunomide, ustekinumab, pembrolizumab, were linked to BP. With the development of checkpoint inhibitors that specifically target the proteins known as programmed cell death protein-1 (PD-1) and programmed death ligand-1 (PD-L1), immunotherapy has become an increasingly popular adjuvant treatment for patients with metastatic cancers. Immunomodulator agents such as pembrolizumab enhance T-cells mediated immune response, which could lead to autoimmune diseases. The most commonly reported is bullous pemphigoid. PD-1 and PD-L1 inhibitors pembrolizumab, nivolumab, and durvalumab are most frequently associated with bullous pemphigoid. Pembrolizumab is a programmed cell death protein (PD-1). PD-1 stimulates the immune system by reversing T-cell inhibition. The exact pathophysiology of immunotherapy-associated bullous pemphigoid is unknown, theories include the presence of the common BP180 antigen on tumor cells, B- and T-cell activation, and the generation of secondary autoantibodies.<sup>2,27</sup> The development of bullous pemphigoid disease may be brought on by anti-PD1's ability to break down the PD1/PDL1 pathway's defense against T-cell-mediated autoimmunity. Simultaneously, alternative hypotheses suggested that anti-PD1 contributed to the enhancement of the antigen-specific antibody response that is initiated by B cells. To fully understand the pathogenetic mechanism of these medications in bullous pemphigoid disease, more research is required.<sup>6</sup>

Bullous pemphigoid was associated with various vaccines, like influenza, poliomyelitis, diphtheria, meningococcus, hepatitis B, rabies, tetanus toxoid, and herpes zoster virus.<sup>6,28</sup> More recently, following the injection of SARS-CoV-2 vaccinations, there have been reports of both new onset and reactivation of bullous pemphigoid. The clear pathogenesis of SARS-CoV-2 vaccination-associated bullous pemphigoid was still unclear. Vaccine-induced immune activation could be a contributing factor. But as of right now, no proteins in the basement membrane are known to be structurally identical to SARS-CoV-2. More recently, information about the interactions between tissue proteins transglutaminase TGase2 and TGase3, and antibodies to the SARS-CoV-2 spike protein, has been published. It has been proposed that cross-reactivity between these particles leads to the development of autoimmune diseases such as bullous pemphigoid.<sup>29</sup> In our study, mRNA Covid-19 vaccine (Pfizer) was linked to BP. Pfizer vaccine is more often associated with vaccine-induced bullous pemphigoid than other mRNA-or vector-based vaccines. SARS-CoV-2 vaccinations induced bullous pemphigoid may be caused by a particular pathogenetic process in individuals with genetically predisposed. The predominant serological feature of vaccine-associated BP linked to SARS-CoV2 is the existence of autoantibodies against BP180. Maronese et al study found that 17 patients out of 21 patients with vaccines-associated bullous pemphigoid received the Pfizer vaccine.<sup>28</sup>

In our study, doxycycline, a tetracycline antibiotic was reported had been linked with bullous pemphigoid. Drugs-associated bullous pemphigoid was rather uncommonly caused by antibiotics. Liu et al study found that antibiotics were not significantly associated with bullous pemphigoid. Many theories have been put forth to try and explain the BP caused by antibiotics, but the processes are not entirely known. A few possibilities concern the medications' chemical structures. Medication containing sulfhydryl molecules (thiols: penicillamine, captopril, penicillin and its derivatives, furosemide, and some cephalosporins) can either directly disrupt the DEJ without immune mediation or can cause an immune system dysregulation that results in autoantibodies being released against the basement membrane zone and disruption of T-

suppressor cell function. Furthermore, thiol medications may cause direct, non-immunogenic harm to the dermo-epidermal interface, thereby exposing the immune system to novel antigens. Some drugs, like aspirin and some cephalosporins, have a phenol ring. Nonthiol nonphenol drugs, like most nonsteroidal anti-inflammatory drugs and angiotensin-converting enzyme inhibitors other than captopril, can interfere with the antigenicity molecules of the DEJ by acting as a hapten that triggers the formation of specific antibodies that cause bulla.<sup>1,6,7,30</sup>

One article included in our systematic review showed that torsemide, a diuretics, was linked with bullous pemphigoid. One of the most often mentioned medications as a potential cause of bullous pemphigoid illness is diuretics. Diuretics are typically prescribed to elderly individuals because of long-term cardiovascular conditions. When a side effect arises, this could result in many treatment difficulties within the same medication family. A number of diuretic families, including loop diuretics (bumetanide and furosemide), thiazides, and potassium-sparing diuretics (spironolactone, an aldosterone antagonist, and the epithelial sodium channel blockers triamterene), have been linked to bullous pemphigoid as an adverse medication reaction.<sup>6</sup> Liu et al study found that the use of aldosterone antagonists was significantly associated with bullous pemphigoid, but no significant associations of thiazides and loop diuretics with bullous pemphigoid.<sup>1</sup> The case report of Helm et al reported elderly patients with a history of atrial fibrillation, cardiomyopathy, diabetes, pacemaker placement, hip replacement surgery, and chronic lymphocytic leukemia were diagnosed with bullous pemphigoid after consumption of furosemide for several months.<sup>31</sup>

## CONCLUSION

Our study suggests that dipeptidyl peptidase-4 inhibitors and aldosterone antagonists are associated with BP. Other medications, such as immunomodulatory agents, anticonvulsants, tyrosine kinase inhibitors, antibiotics, anticoagulants, diuretics, and mRNA COVID-19 vaccine, may be associated with BP. However, further study with larger samples was needed. Regarding these results, clinicians should pay close attention to prescribing the medicine to their patients.

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