

## Descriptive Profile of Anaphylactic Reaction Patients Hospitalized at RSUP Prof. DR. I.G.N.G Ngoerah Period 2018-2023

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### KEYWORDS

Anaphylactic reaction;  
anaphylactic shock; clinical  
profile; clinical manifestation

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### ABSTRACT

**Introduction:** Anaphylactic reaction is a severe, potentially life-threatening systemic hypersensitivity reaction caused by a specific allergen. This study aimed to evaluate the clinical profile of anaphylactic patients hospitalized in Prof. Dr. I.G.N.G. Ngoerah Hospital, Denpasar. **Method:** This was a cross-sectional descriptive study of anaphylactic patients hospitalized in our center from January 2018 to December 2023. Patients diagnosed with anaphylactic reactions were included in this study. All the data (demographic, clinical manifestations, potential trigger) were attained from medical records for descriptive analysis. **Result:** 292 patients were enrolled in this study; half were women (54,4%), and the median age was 38,50 years (interquartile range 24). The most common potential triggers were drugs (57%), followed by food (18,5%), blood products (14,1), insect bites, and other triggers (4,8%). Almost all patients experience skin and mucosal manifestations (99%). Anaphylactic shock occurs in only 22% of patients. **Discussion:** Previous studies have found similar results to our findings, and anaphylactic reaction caused by drugs was associated with a more severe reaction. The effect of estrogen hormones on more severe reactions has been reported in female mice, but human research is still limited. **Conclusion:** Further studies are needed to investigate the correlation between demographic characteristics or specific clinical manifestations with a severe reaction

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### 1. Introduction

Anaphylactic reactions are systemic allergic reactions that involve one or more organ systems and occur in seconds to minutes, potentially life-threatening. Anaphylactic reactions are most often triggered by medications, foods, and other Hymenoptera or triggers such as contrast agents and latex exposure (Hong & Boyce, 2018). Most anaphylactic reactions are uniphasic, and about 10-20% of cases are biphasic, where anaphylactic symptoms may reappear an hour or a few hours after the

resolution of the initial symptoms (Hong & Boyce, 2018). Cutaneous is the most common clinical manifestation, including very itchy urticaria eruptions, diffuse erythema, and warm palpation. Gastrointestinal manifestations include nausea, vomiting, abdominal pain, and fecal incontinence. Cardiovascular and respiratory manifestations are manifestations of life-threatening anaphylactic reactions. Laryngeal edema will be felt like a mass in the throat, hoarseness, or stridor, while bronchial obstruction will be felt like suffocation or chest tied with/without wheezing (Hong & Boyce, 2018).

The incidence of anaphylactic reactions worldwide ranges from 50 to 112 episodes/100,000 inhabitants each year, and the lifetime prevalence ranges from 0.3-5.1% (Tanno et al., 2018). Recurrence occurs in 26.5%-54% of patients with a previous anaphylactic reaction followed for 1.5-25 years (Tejedor-Alonso et al., 2015). The mortality rate due to anaphylaxis is relatively low, which is estimated at 0.05-0.51/1 million population/year due to drugs, 0.03-0.32 due to food, and 0.09-0.13 due to poison from insect bites (Ansotegui et al., 2016). Anaphylactic reactions account for 0.26% of the causes of hospitalization (Asai et al., 2014). In the United States, less than 20% of anaphylactic patients are hospitalized, while higher rates are reported in the United Kingdom as national guidelines recommend hospitalization for all cases of anaphylaxis (Anagnostou & Turner, 2019; Motosue et al., 2018). This difference in numbers is due to the difference in the criteria for anaphylactic reactions that require hospitalization in several countries. This study aims to determine the descriptive profile of anaphylactic reaction patients at Prof. Ngoerah Hospital from 2018 to 2023.

## 2. Materials and Methods

This study used a cross-sectional research design involving 292 patients. The sampling technique used in this study was total sampling. The study included patients with a diagnosis of anaphylactic reactions who were hospitalized at Prof. Dr. I.G.N.G. Ngoerah Hospital, Denpasar, Bali, from January 2018 to December 2023.

The data in this study used secondary data taken from the medical records of all patients with a diagnosis of anaphylactic reactions (meeting the NIAID/FARE anaphylaxis criteria) (Sampson et al., 2006). The data collected included demographic characteristics such as age and gender, clinical manifestations, and allergens that trigger anaphylactic reactions. Allergens are differentiated into drugs, food, insect stings, and others (such as contrast agents, blood products, latex, and airborne allergens that exercise induces). Patient complaint data is the basis for grouping clinical manifestations. Manifestations of the skin, mucosal tissue, or both include urticaria generalis, pruritus or redness, swelling of the lips-tongue-uvula. Respiratory manifestations include dyspnea, wheezing or bronchospasm, stridor, and hypoxemia. Gastrointestinal manifestations include abdominal pain, diarrhea, nausea, and persistent vomiting. Cardiovascular manifestations include a decrease in blood pressure or syncopagus. In addition, the frequency distribution of anaphylactic reaction events and anaphylactic shock was also observed. The data obtained is presented in the form of tables and bar charts. The data was analyzed using SPSS® version 25 software.

## 3. Result and Discussion

Based on 292 medical record data of patients with a diagnosis of anaphylactic reactions who were hospitalized at Prof. Dr. I.G.N.G. Ngoerah Hospital, Bali, from January 2018 to December 2023,

the median age was 38.50 years (interquartile range 24). There were more female patients than males, 159 patients (54.4%) and 133 patients (45.5%), respectively (**Table 1**).

The most common triggering allergens are drugs (57%), followed by food (18.5%), blood products (14.1%), insect stings, and other triggers (4.8%), such as dust, COVID-19 vaccines, and contrast agents. Antibiotics and OAINS are the most commonly found drugs to cause anaphylactic reactions, namely 17.5% and 15.1%, respectively (**Table 2**). Almost all patients diagnosed with anaphylactic reactions experience skin and mucosal manifestations (99%). The second most common clinical manifestation was respiratory (46.6%), followed by cardiovascular (24.7%) and gastrointestinal (10.6%) (**Figure 1**). Anaphylactic shock is only found in 22% of patients. A total of 45.9% of patients experienced acute hypersensitivity reactions, and another 31.8% experienced anaphylactic reactions (**Figure 2**).

## Discussion

The demographic characteristics of this study were similar to those of the study in Japan, where more than half of the patients were female (60.3%), but the median age reported was lower at 32 years (IQR 13-37). The average age of patients with anaphylactic reactions in other studies varied, namely 32 years and 40.5 years, with the majority being female (Liu et al., 2020; Poziomkowska-Gęszicka & Kurek, 2020).

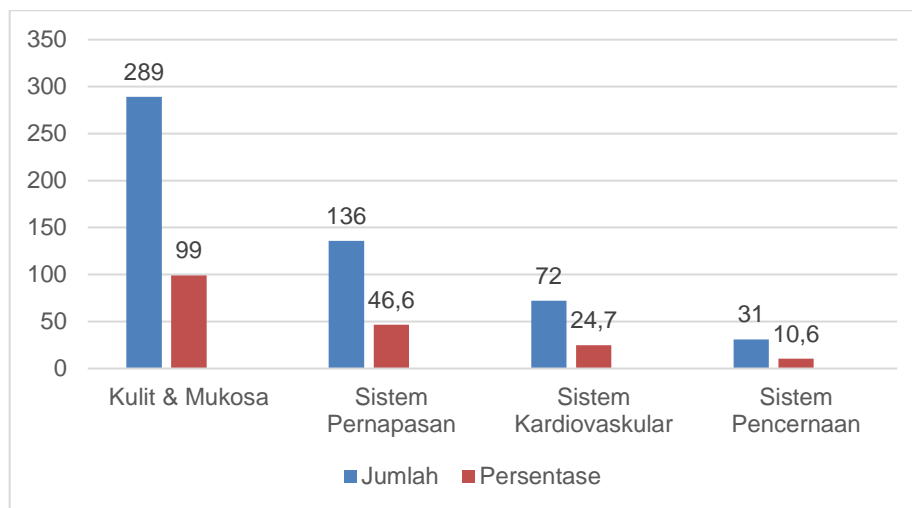
**Table 1 Demographic Characteristics of Patients**

Variable	Value
Age (median (IQR))	38,50 (24)
Gender, n (%)	
Male	133 (45,5%)
Female	159 (54,5%)

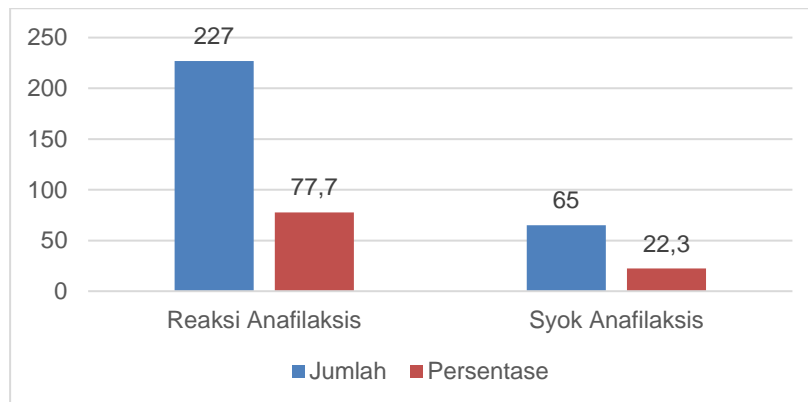
**Table 2 Types of triggering allergens**

Variable	Value (n(%))
Medicine	169 (57%)
Antibiotik	51 (17,5%)
Antivirus	1 (0,3%)
Non-steroidal anti-inflammatory drugs (OAINS)	44 (15,1%)
Paracetamol	17 (5,8%)
Anti-seizure	11 (3,8%)
Anti-hypertension	1 (0,3%)
Anti-platelet	2 (0,7%)
Fibrinolitik	1 (0,3%)
Anti-tuberculosis drugs (OAT)	20 (6,8%)
Antiretroviral drugs (ARV)	8 (2,7%)
<i>Proton pump inhibitor</i> (PPI)	3 (1%)
Mucolytic	1 (0,3%)
Bronchodilator	1 (0,3%)
Corticosteroid	1 (0,3%)

Chemotherapy	2 (0,7%)
Metamizole	1 (0,3%)
Metformin	1 (0,3%)
Somatostatin	1 (0,3%)
Food	54 (18,5%)
Insect sting	14 (4,8%)
Blood products	41 (14,1%)
Others	14 (4,8%)
Dust	1 (0,3%)
Adult COVID-19	4 (1,4%)
Contrast Agents	9 (3,1%)



**Figure 1** Distribution of frequency of clinical manifestations of anaphylactic reactions



**Figure 2** Distribution of frequency of clinical manifestations of anaphylactic reactions

In a retrospective study on the anaphylactic reaction profile in Surabaya, the male sex was more found in the <15-year-old patient group (68.75%), while in the >15-year-old patient group, the female gender was more found (75%) (Hasanah et al., 2020). The hormone estrogen regulates the expression of endothelial nitric oxide synthase (eNOS) and nitric oxide production, increasing vascular permeability and aggravating anaphylactic reactions in female rats. Exacerbations of

anaphylactic reactions can be prevented by the administration of estrogen receptor antagonists or ovariectomy, but exacerbations occur after the administration of estradiol in female rats undergoing ovariectomy (Hox et al., 2015). However, research on the effect of female sex hormones on the severity of anaphylactic reactions in humans is limited. Previous research has also linked age to the severity and fatality of anaphylactic reactions. Increasing age is associated with more severe anaphylaxis and hospitalization rates (Clark et al., 2014).

Several other studies have also found that drugs are the most common triggering allergen, with antibiotics being the most widely reported triggering allergen (Hasanah et al., 2020; Wood et al., 2014). The United States and Australia reported increased fatalities due to drug-induced anaphylaxis (Jerschow et al., 2014; Mullins et al., 2016). The incidence of drug-induced anaphylactic reactions reported by a study in the United Kingdom was 42% (González-Pérez et al., 2010). Based on data in Vietnam from 2010 to 2016, there has been an increase in cases of drug-induced anaphylaxis, especially antibiotics. A retrospective study at a hospital in Surabaya reported that the antibiotics that cause anaphylactic reactions are penicillin, third-generation cephalosporins, and quinolones (Hasanah et al., 2020). One of the most extensive studies in the United States found that antibiotics and analgesics were the most common drugs for anaphylactic reactions. Antibiotics that cause anaphylactic reactions include penicillin, sulfonamides, cephalosporins, macrolides, fluoroquinolones, and tetracyclines. OAINS, opioids, and local anesthetics are some of the analgesics that have been reported to trigger anaphylactic reactions (Dhopeshwarkar et al., 2019). Anaphylactic reactions triggered by high-risk drugs are more severe than other triggers (Regateiro et al., 2020). Drug-induced anaphylactic reactions are associated with cardiopulmonary arrest or cardiopulmonary resuscitation (*odds ratios* 1.80 and 2.25, respectively) (Clark et al., 2014). An observational study in Japan found different results, with food allergens being the most common trigger (76.2%), followed by drugs (10.9%) and contrast agents (4%) (Oya et al., 2020).

Previous studies have also reported the most common skin and mucosal manifestations experienced by patients with anaphylactic reactions (Hasanah et al., 2020; Oya et al., 2020). In >90% of anaphylactic cases, cutaneous manifestations are clinical manifestations, including very itchy urticaria eruptions, diffuse erythema, and warm palpation. Urticaria eruptions can appear localized or scattered and rarely persist for 48 hours (Hong & Boyce, 2018). However, cutaneous manifestations are not found in 20% of children with anaphylactic reactions due to food or insect stings.

Observational studies in Japan reported a lower incidence of anaphylactic shock of 13.6%.<sup>20</sup> Some literature has different definitions of anaphylaxis, stating that anaphylaxis must involve several organ systems. However, severe symptoms can appear when only one organ system is involved (Sampson et al., 2006) (Brown et al., 2013). According to Sampson et al., if any of the three criteria are met, then it is most likely anaphylaxis, including (1) acute ankles involving the skin, mucosal tissue, or both (urticaria generalization, pruritus, swelling of the lips-tongue-uvula) and at least meeting one of the following: (a) respiratory manifestations (dyspnea, wheezing, stridor, decreased *peak inflammatory flow*, hypoxemia), (b) Decrease in blood pressure or related to *end-organ* dysfunction (hypotony (fainting), syncope and incontinence); (2) meet two or more of the following that occur immediately after exposure to suspected allergens in patients (minutes to

several hours): (a) skin-mucosal tissue involvement, (b) respiratory manifestations, (c) decreased pressure and associated symptoms, (d) persistent gastrointestinal symptoms (abdominal pain, vomiting); (3) a decrease in blood pressure after exposure to suspected allergens in patients (minutes to several hours) (Sampson et al., 2006).

The World Allergy Organization's 2019 anaphylaxis guidelines simplify the anaphylaxis criteria by combining the two Sampson criteria and modifying the third criterion, namely: (1) acute irritation involving the skin, mucosal tissue, or both (urticaria generalization, pruritus, swelling of the lips-tongue-uvula) and at least meeting one of the following: (a) skin-mucosal tissue involvement, (b) respiratory manifestations, (c) decreased pressure and symptoms related, (d) persistent gastrointestinal symptoms (abdominal pain, vomiting); (2) acute onset of hypotension, bronchospasm or laryngeal involvement (stridor, voice changes, and odynophagia) after exposure to suspected allergen exposure in patients, even without skin involvement (Cardona et al., 2020). Patients with anaphylaxis require more extended observation (24 hours or more) to anticipate biphasic reactions that may occur in the first 6-12 hours after the first reaction appears (Cardona et al., 2020; Oya et al., 2020). Some risk factors associated with biphasic reactions include severe initial reactions, wide pulse pressure at the initial reaction, increased need for epinephrine to cope with the initial reaction, and delayed administration of epinephrine (Turner et al., 2020).

#### 4. Conclusion

In this study, most anaphylactic reaction patients were female, with a median age of 38.50 years (IQR 24). Drugs are the most common trigger allergens, followed by food, blood products, insect stings, and other triggers. Almost all patients diagnosed with anaphylactic reactions experience skin and mucosal manifestations, and anaphylactic shock occurs in only 22% of patients. Further research is needed to determine the relationship between specific demographic characteristics or clinical manifestations and severe reactions. The clinical implications of these findings include: The need for greater vigilance against anaphylactic reactions in female patients of reproductive age, especially when administering medications. The importance of anamnesis of a detailed history of drug allergy before the administration of therapy, especially antibiotics and OAINS which are frequent triggers. Although skin and mucosal manifestations are very common, medical personnel need to be aware of the possibility of asymptomatic skin anaphylaxis, especially in drug-induced cases. The need to educate patients and families about the recognition of early symptoms of anaphylaxis, considering the potential for biphasic reactions. The importance of providing and training in the use of auto-injectors of epinephrine in patients with a history of anaphylaxis, especially those triggered by drugs.

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