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Pattern of Autoimmune Bullous Disorders Based on Histopathological Diagnosis, in ALERT Hospital, Addis Ababa, Ethiopia 2021: An Eight Years (2014-2021) Retrospective Study

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Advisor's approval sheet

This is to verify the thesis entitled "*Pattern of Autoimmune Bullous Disorders Based on Histopathological Diagnosis, in ALERT Hospital, Addis Ababa, Ethiopia 2021: An Eight Years (2014-2021) Retrospective Study"* is submitted in partial fulfillment of the requirements for the Specialty Certificate in Dermatovenereology to the graduate program of the school of Medicine in Addis Ababa University and has been carried out by Yohannes Tadesse under our supervision.

The student has fulfilled the thesis requirements and hence here by can submit the thesis to the school.

Name of advisor:……. Date…… Signature……..

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Examiners' Approval Sheet

We, the undersigned members of the Board of Examiners of the final open defense by Yohannes Tadesse , have read and evaluate this thesis *"Pattern of Autoimmune Bullous Disorders Based on Histopathological Diagnosis, in ALERT Hospital, Addis Ababa, Ethiopia 2021: An Eight Years (2014-2021) Retrospective Study".* This is to verify that the thesis has been accepted in partial fulfillment of requirements for the Specialty Certificate in Dermatovenereology to the graduate program of the school of Medicine in Addis Ababa University.

Name of examiner ……. Date…… Signature……..

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Acknowledgement

I would like to thank Addis Ababa University; School of Medicine, Department of Dermatovenereology for giving me an opportunity to prepare this research proposal. A special gratitude to ALERT/AHRI for allowing me to conduct this study.

List of Abbreviations and acronyms

AHRI: Armauer Hansen Research Institute

AIBD: Autoimmune Bullous Diseases/Disorders

ALERT: All African Leprosy, Tuberculosis and Rehabilitation Training Center

BP: Bullous Pemphigoid,

CI: Confidence Interval

DH: Dermatitis Herpetiformis

EBA: Epidermolysis Bullosa Acquista

ETB: Ethiopian Birr

FS : Fogo Selvagem

LAD: linear IgA Dermatosis

MMP: Mucous Membrane Pemphigoid

PF: Pemphigus Foliaceus

PG: Pemphigoid Gestationis

PI: Principal Investigator

PV: Pemphigus Vulgaris

Abstract

Background: Autoimmune bullous diseases are a group of rare, acquired disorders causing blistering of the skin and/or mucous membranes characterized by overlapping features, resistance to treatment, and run a chronic course associated with significant morbidity and mortality. The incidence of autoimmune bullous diseases among the general population is reported as 14.5/million/year. Therapy of bullous diseases consists of suppressing the immune system, controlling inflammation and improving healing of erosions. Majority of autoimmune bullous diseases are chronic diseases that can cause physical and emotional distress which is exacerbated by the need to often have lifelong treatment with immunosuppressive therapies that have potentially severe adverse effects. To the knowledge of the investigator, there is no study conducted regarding the prevalence of auto immune bullous diseases in Ethiopia.

Objective: Assess the pattern of autoimmune bullous diseases based on histopathological diagnosis in ALERT/AHRI hospital from 2014-2021

Methods: A retrospective cross sectional study was conducted at ALERT/AHRI. Histopathologic reports of all patients from January, 2014- June, 2021 were reviewed and cases with autoimmune conditions were selected. Obtained data were coded and entered using Epi-Data version 4.6.0.2, and it was cleaned and analyzed using SPSS. Descriptive analysis of basic participant's characteristics and disease pattern of autoimmune disease was conducted.

Result: From the 13,563 patients sent for biopsy analysis, 134 patients were sent for histopathology confirmatory test for AIBD in the study period, 86 study participants who full fill the operational definition were enrolled and analyzed. Among these 37.2% of them were male and the rest 62.8% were female, with a mean age of 40.9 year, the minimum age of disease onset being 7 month of age and the maximum age of disease onset was 82 years old. The most frequent AIBD was Bullous pemhigoid with 34.8% (n=30), followed by pemphigus foliaceous and pemphigus vulgaris each being 24.4% (n=21).

Conclusion and recommendations: This study found bullous pemphigoid is the most prevalent in the assessed institution site. The overall mean age of the patients being 40.9 years, with a minimum age of 7 month and maximum of 82 years. Moreover, AIBD was seen in higher predominance in female patients, it is recommended for researchers to conduct a prospective study including other hospitals with a clinical correlation plus a qualitative study to assess how to improve the quality of life for such patients. Moreover, it is recommended to use a confirmatory diagnosis of AIBD i.e. immunofluorescence study for further researches.

1. Introduction

1.1 Background

Autoimmune bullous diseases(AIBD) are a group of rare, acquired disorders causing blistering of the skin and/or mucous membranes characterized by overlapping features, resistance to treatment, and runs a chronic course associated with significant morbidity and mortality. AIBD occurs when the body's immune system mistakenly attacks healthy tissue in which antibodies erroneously attack proteins that are essential for the layers of skin to adhere together (1).

Based on pathogenesis, bullous skin diseases can be divided into autoimmune and non-autoimmune bullous skin diseases. In autoimmune bullous diseases, pathogenic autoantibodies can be detected in both the circulation and skin lesions, while genetic factors play a more significant role in the pathogenesis of non-immune bullous skin diseases while based on the affected skin layer it can be further classified into intra- epidermal and subepidermal bullous skin diseases (2). Clinically, there are several different categories of autoimmune blistering diseases including pemphigus, pemphigoid, IgA-mediated dermatoses and epidermolysis bullosa acquisita (EBA). Pemphigus can be further classified as pemphigus vulgaris(PV), pemphigus foliaceus(PF) and paraneoplastic pemphigus; pemphigoid is further classified as bullous Pemphigoid(BP), mucous membrane pemphigoid(MMP), pemphigoid gestationis(PG); IgA-mediated dermatoses is also classified as Dermatitis herpetiformis(DH) and linear IgA(LAD) (1,3).

The incidence of AIBD among the general population is reported as 14.5/million/year. Pemphigus vulgaris and bullous pemphigoid are the most frequently reported autoimmune bullous diseases ranging from 0.76 per million population per year in Finland to 16 per million per year in Israel, and the incidence of pemphigus foliaceus varies between 0.5 and 1.0 per million per year in Western Europe and 6.7 per million per year in Tunisia. The incidence of dermatitis herpetiformis has been estimated at 10 in 100,000. The exact incidence of epidermolysis bullosa acquisita and the pemphigoid disorders is unknown. (1,4,5). High incidence of autoimmune bullous diseases in some ethnic groups such as pemphigus in

Ashkenazi Jewish, or as pemphigus foliaceus in Brazil has been shown to be related to genetic and environmental factors, respectively. AIBD affects men and women in equal numbers. Most forms occur in middle-aged individuals, usually people in their 50s and 60s, though it can affect individuals of any age including children (1,4).

The clinical features of AIBD are heterogeneous and may present with erythema, blisters and bullae in the skin and mucous membranes, evolving into erosion and ulcers after rupture. This leads to severe complaints for the patients and increased risk of pain, dysphagia, water loss, electrolyte imbalance and infections (2,6).

A diagnosis of AIBD is suspected based upon identification of characteristic findings, a thorough clinical evaluation. The diagnosis may be confirmed based upon performing two biopsies, one for light microscopy and the other for DIF; conducting blood tests to reveal the characteristic antibodies associated with specific AIBD; direct immunofluorescence microscopy (DIF) and performing microbiological diagnostics to test for infectious causes. The gold standard test to diagnose AIBD is direct immunofluorescence microscopy and collecting a serum sample for immune serological tests (1,6).

Although there is no cure for autoimmune blistering diseases, they can often be controlled with treatment. Therapy of bullous diseases consists of suppressing the immune system, controlling inflammation and improving healing of erosions. The mainstay of treatment is corticosteroids. Either alone or in combination with other drugs have been used to treat individuals with AIBD. These drugs include drugs that suppress the immune system such as mycophenolate, azathioprine or cyclophosphamide, immunosuppressive biological therapies such as rituximab, and intravenous immunoglobulin G (1,7).

1.2 Statement of the problem

Active disease and past damage from AIBD can cause significant morbidity and negatively impact on the patient's function (8). Physical symptoms including pain and itch, disfigurement due to blistering and scarring causes reduced functional capacity that is imposed by disability and the economic burden and side effects that are associated with treatment all contribute to the burden of these diseases (9). Moreover, mortality risk of the patients with bullous pemphigoid was found at least 2 times higher and the mortality risk of the patients with pemphigus was found approximately 3 times higher than that of the general population(4). A study from Taiwan showed that survival in patients diagnosed with pemphigus was significantly lower than that expected in the general population. Overall, patients with pemphigus had a 2.36-fold increase in mortality compared with the general population (7).

Regarding quality of life, the majority of AIBDs are chronic diseases that can cause physical and emotional distress which is exacerbated by the need to often have lifelong treatment with immunosuppressive therapies that have potentially severe adverse effects. A hospital-based study in Morocco showed among patients with pemphigus, 70% reported enormous shame about their appearance, 60% were anxious about negative reactions from others, and 63% had a significant loss in confidence, including concerns about the impact of the disease on sexual function. Social misconceptions may also contribute to the higher psychological morbidity that is observed in female patients (9, 10).

To the knowledge of the investigator, there is no study conducted regarding the prevalence of AIBD in Ethiopia.

1.3 Significance of the study

This retrospective study will generate local knowledge regarding the prevalence of AIBD associations with age and sex at ALERT/AHRI hospital and it will serve as a landmark to conduct bigger epidemiological studies. In addition, other studies regarding the quality of life related with AIBD chronicity and management side effects and studies regarding environmental and genetic factors that play an important role in a predisposition to AIBDs can be conducted

2. Literature Review

In Uganda, a retrospective study from May 2000 to June 2002 was conducted to assess autoimmune subepidermal blistering diseases and correlation of autoantibody class with age of patients. The diagnosis was based on the clinical presentation and on the presence of circulating autoantibodies detected by indirect immunofluorescence microscopy. The result showed, 22 patients with autoimmune subepidermal blistering skin disorders, including nine with BP (41%), four with linear immunoglobulin A (IgA) disease (18%), three with mucous membrane pemphigoid (14%), two with linear IgG/IgA bullous dermatosis (9%), and one each with cicatricial pemphigoid and epidermolysis bullosa acquisita (5%). In patients with subepidermal blistering diseases, IgG reactivity correlated significantly with old age, whereas younger patients preferentially developed IgA autoantibodies ($P = 0.024$) (11).

In South Africa, a 12 years prospective study was conducted to describe the demography, prevalence, clinical features, response to treatment, and human leukocyte antigen (HLA) characteristics of pemphigus. All patients with pemphigus were recruited over 12 years from January 1987 to December 1999. As a result 112 patients had pemphigus. PF was the commonest variant seen (62 patients) and 80% of these patients were black. The mean age was 43 years (12–93 years) and the male to female ratio was 1: 1.4. Fifty patients had PV, of whom 82% were Indian. The mean age of presentation of PV was 48 years (21–82 years). The male to female ratio was 1: 1.7. The mortality rate was 14% in the total sample (six in PV and two in PF). HLA-B8 was positive in 41% of patients with PF ($P < 0.001$) (12).

An 11-year (1997-2007) retrospective study conducted in Tunisia to assess the spectrum of AIBD involving 174 patients revealed, Pemphigus was observed to be the most common AIBD (53%), with the majority being PV(61%) vs. 36% of PF (Tunisian pemphigus) (13).

In Saudi Arabia a retrospective data between 1997 and 2016 was obtained to analyze histologic characterization of cellular infiltration in autoimmune subepidermal bullous diseases in a tertiary hospital and biopsy-based data collected from 65 patients. This study reveals a total of 65 cases of autoimmune subepidermal bullous diseases were diagnosed based on the histopathology features and direct immunofluorescence assay on skin biopsies. The most common cause was BP

(38%), followed by PG (34%), LAD (6%), Bullous Lupus Erythematosus (6%), EBA (6%), DH (5%), Lichen Planus Pemphigoid (3%), and Bullous Vasculitis (2%) (14).

In Iran, a 13-year retrospective study was designed to evaluate Spectrum of AIBD diseases from documented data obtained from hospitalized patients with AIBDs from October 1999 to October 2012. From 168 patients, 78% had pemphigus. The age of patients at presentation ranged from 1 month to 115 years, with a mean of 47.5±19.93 years. Mucosal or skin involvement of AIBDs was statistically significant (P, 0.001). The incidence of AIBDs differed significantly based on anatomic location (P=0.003) and three deaths were documented (15).

In Taiwan, a nationwide population-based study was conducted on the incidence, mortality, and causes of death of patients with pemphigus. In this cohort 853 patients with pemphigus who were first diagnosed between 1 January 2002 and 31 December 2009, were included. Among which, 366 (42.9%) were male and 487 (57.1%) female patients. The mean age of onset of pemphigus was 52.5±15.9 years (median, 51 years). The average incidence rate of pemphigus was 4.7 (95% CI, 3.2–6.2) per million per year. The incidence was higher in women, at a rate of 5.4 (95% CI, 3.6–7.3) per million per year, than in men, at a rate of 4.0 (95% CI, 2.7–5.2) per million per year (P<0.001). People aged 60 years and older had the highest risk of developing pemphigus, with an incidence rate of 11.9 (95% CI, 6.2–17.5) and 10.5 (95% CI, 6.7–14.3) per million per year for men and women, respectively. The lowest incidence of pemphigus was seen in patients less than 40 years of age, with a rate of 1.4 (95% CI, 0.7–2.0) and 2.0 (1.1–2.9) per million per year for men and women, respectively. A total of 88 patients (10.3%) died during the study period, of whom 54 were male and 34 were female (5).

In France, a retrospective cohort study conducted on the incidence and mortality of BP, 542 patients were identified from the database of pathology laboratories from the three university hospitals and four general hospitals, and 58 cases from the four private-practice laboratories of the three regions from 2000-2005. A total of 502 incident cases of BP (305 women, 197 men) were included. Mean age at diagnosis was 82.6±8.8 years with range from 49 to 106 years. Distribution of patients according to age and sex appeared similar in the three regions (*P*=0.63 and *P*=0.24, respectively). Overall, 92 percent of incident BP cases were aged 70 years or above and 46% were aged 85 years or above (16).

In Spain, the prevalence of AIBDs is around 40 cases per million persons per year for bullous pemphigoid, and 7 cases per million persons per year for pemphigus vulgaris. In a hospital based review study from 2000-2011 found, a total of 61 patients with the following diagnoses and distribution: 36 with PV (59%), 4 with PF (7%), 10 with BP (16%), 6 with MMP (10%), and 5 with dermatitis herpetiformis (8%). from a mail and e-mail epidemiologic survey on PV conducted at 26 dermatology departments, the estimated incidence was 2.4 cases per million people per year, and a prevalence of 23 cases per million people per year. Most patients with AIBD in Spain are diagnosed based only on clinical and histologic criteria. Immunofluorescence techniques (both direct and indirect) are largely unavailable in most small and middle-sized hospitals (17).

A population based cohort study conducted in UK regarding incidence and mortality of Bullous pemphigoid (869 people) and pemphigus vulgaris (138 people) with pemphigus found the median age at presentation for bullous pemphigoid was 80 (range 23-102) years, and 534 (61%) patients were female. The median age at presentation for pemphigus vulgaris was 71 (21-102) years, and 91 (66%) patients were female. Incidences of bullous pemphigoid and pemphigus vulgaris were 4.3 (95%CI 4.0 to 4.6) and 0.7 (95%CI 0.6 to 0.8) per 100 000 person years. The average yearly incidence increase of bullous pemphigoid was 17% (incidence rate ratio=1.2, 95%CI 1.1 to 1.2), while for pemphigus vulgaris was 11% (incidence rate ratio=1.1, 1.0 to 1.2) occurred. The risk of death for patients with bullous pemphigoid was twice as great as for controls (adjusted hazard ratio=2.3, 95% CI 2.0 to 2.7). For pemphigus vulgaris, the risk of death was three times greater than for controls (adjusted hazard ratio=3.3, 2.2 to 5.2).The crude incidence of bullous pemphigoid was 4.28 (95% confidence interval 4.01 to 4.58) per 100 000 person years. Incidence increased with age. In the case of Pemphigus vulgaris the crude incidence was 0.68 (0.58 to 0.80) per 100 000 person years. Incidence was higher in women and in older age groups. An estimated 11% increase in incidence per calendar year (incidence rate ratio 1.11 (1.04 to 1.17) per year; P=0.001) was found (18).

The prevalence of AIBD in calculated based on the ICD-coding-based dataset in Germany revealed about 40,000 AIBD patients including 21,000 patients with BP, 7,700 with PV, and around 2,000 with MMP (13). Another study conducted in Germany on the prevalence of Pemphigus and Pemphigoid states, a prevalence of bullous pemphigoid of 259 cases per million

people in a single tertiary referral center in Lower Franconia, Germany. The age distribution of major AIBDs, bullous pemphigoid and mucous membrane pemphigoid were more frequent in the elderly population, whereas pemphigus diseases predominantly occurred in middle age. Although it is known that most cases of epidermolysis bullosa acquisita affect the elderly, the second peak of disease onset in the first three decades of life were seen (19).

PV is considered the most severe form of pemphigus, it accounts for 70% of pemphigus cases. It is a rare disease, with an annual incidence that varies between 0.76 cases/million in Finland and 16.1 cases/million in Israel, depending on the study population. It primarily affects adults, between the fourth and sixth decades of life. In Brazil, it also develops in young adults. Most studies have noted a higher incidence in women, with the female: male ratio ranging from 1.1 (Finland) to 5.0 (US). In Brazil, its incidence is high, mainly in the Midwest and northwest regions, and is called endemic PF or FS. This differs from classical pemphigus foliaceus, based on its epidemiology: it compromises young adults from the rural areas of Fogo selvagem regions, with a family history (20).

Bullous pemphigoid is the most common form of AIBD of the skin and mucous membranes. It has an estimated prevalence of 1/4,000 in Europe. Its incidence reaches around 20/million/year in Central Europe. The incidence is reported to be increasing but currently ranges between 2-22/1,000,000 worldwide. This is partly due to the rising life expectancy of the general population, increasing awareness, and enhanced diagnostic tests and close association between BP and neurological diseases, whose incidences are also rising. BP is typically a disease of the elderly with an estimated median age of onset of after 60 years. Although overall incidence is slightly higher in females, after the age of 80 years it is more frequent in males. Some drugs are associated with its onset such as (diuretics, antiarrhythmics, neuroleptics, gliptins, and immunotherapies) (4,21). Moreover, a systematic review and meta-analysis study conducted in china regarding the incidence and Prevalence of BP states the overall estimate of the pooled incidence was 0·1138 per 10,000 person-years. A higher incidence of BP was found in North America, among females and among older people. The incidence values for males and females were 0·0172 (95% CI: 0·0075-0·0396) and 0·01334 (95% CI: 0·0048-0·0221) per 10,000 person-years, respectively. BP is followed by mucous membrane pemphigoid (MMP) and pemphigoid gestationis, with incidences of 2/million/year (22, 23).

The development of autoimmune diseases is generally multi-factorial. Factors involved are a genetic predisposition, ethnicity, age, the environment, and gender bias toward females. The two major groups of AIBDs are: pemphigus and pemphigoid diseases, based on the auto antigen localization. Population-dependent incidence of pemphigus diseases ranges between 0.7 and 5 per million/year. Central Europe and the United States are the highest in incidence ranging for new cases between 1 and 7 per million/year. PV is 4 to 10 times more common among the Jewish population as compared to other Caucasian populations. In contrast, endemic PF-variants have been described in South America and Tunisia (3).

3. Objectives

3.1 General objectives

- Assess the Pattern of Autoimmune Bullous Disorders AIBD based on histopathological diagnosis from January, 2014- June 2021 in ALERT/AHRI hospital, Addis Ababa, Ethiopia.

3.2 Specific objectives

- Determine the disease Pattern of AIBD from January, 2014- June,2021 in ALERT/AHRI hospital, Addis Ababa, Ethiopia.
- Identify the association of AIBD Pattern with age and sex from January, 2014- June 2021 in ALERT hospital, Addis Ababa, Ethiopia.

4. Methodology

4.1 Study area

ALERT is located at Kolfe Keranio sub city, Addis Ababa, Ethiopia. ALERT's activities initially focused on rehabilitation of leprosy patients, training programs on leprosy for personnel from around the world and leprosy control. The hospital currently provides a wide range of services in various departments including Dermatology, emergency services, gynecology and obstetrics, pediatrics, HIV treatment, orthopedics and plastic surgery. It also provides histopathologic study services & teaching activities by general & dermatopathologists & other molecular study services by AHRI/ALERT department. As of 2018, ALERT was attending over 375,000 patients per year; 1200-1500 patients visit the center daily. The department of dermatology hospital offers a full range of dermatologic care for both common and rare problems of skin, hair, nails and mucous membranes. Accordingly, 150,000 dermatology cases have been attended annually (24).

4.2 Study design

A hospital based retrospective cross-sectional study was conducted in which histopathologic reports regarding AIBD elapsing from January, 2014- June, 2021 was obtained from ALERT/ARHI archive.

4.3 Population

4.3.1 Source population

All patients for which biopsy was sent in ALERT hospital during the study period (January, 2014-June, 2021)

4.3.2 Study population

The study population included patients with histopathologic diagnosis of AIBD during the study period (January, 2014- June, 2021)

4.4 Study Variables

Dependent variable:

- Histopathologic profile of AIBD

Independent variables:

- Age
- Sex

Inclusion criteria:

All patients, whose histopathology reports are available and diagnosed with AIBD using histopathological examination,

4.5 Operational definition

Histopathology: a diagnostic modality by microscopic examination of sections of tissue taken by biopsy

Histopathologic diagnosis of AIBD: when the result signed out with " **diagnosis of"** or "**represents"** or "**suggestive of"** specific AIBD

4.6 Sample size

Due to the limited small number of the cases and the nature of the study technique, the investigator has chosen to use non probability sampling. All cases of histopathologic diagnosis of AIBD in the previous eight years

4.7 Data collection procedure and tool

Secondary data regarding the histopathological diagnosis of AIBD, age and sex will be obtained from ALERT/AHRI archive

4.8 Data quality management

Data extraction from histopathologic reports was performed by the principal investigator and trained residents. Obtained data was coded and entered using Epi-Data verion4.6.0.2, and cleaned using SPSS version 20.

4.9 Data analysis

Data was analyzed using SPSS version 20 and descriptive analysis of basic participant's characteristics and disease spectrum of AIBD was performed. The result will be displayed in tables, graphs and percentages.

4.10 Ethical consideration

This research proposal was submitted to Addis Ababa University, School of Medicine, and Dermatovenereology department Ethical Committee for review, then to the IRB of the College of Health sciences & to the ALERT/AHRI Ethics review committee. After Ethical Approval formal letter of cooperation was written to ALERT/AHRI hospital to access patient's histopathological records. Only approved study personnel had access to the medical records. After completion of the study, identifier information was set aside and only study identification number (ID no.) was used during analysis.

5. Result

5.1 Study participants

From January, 2014- June, 2021, a total of 134 patients were clinically suspected to have AIBD and biopsy was sent. From those 134 suspected patients, 86 found to have AIBD on histopathology (Figure 1).

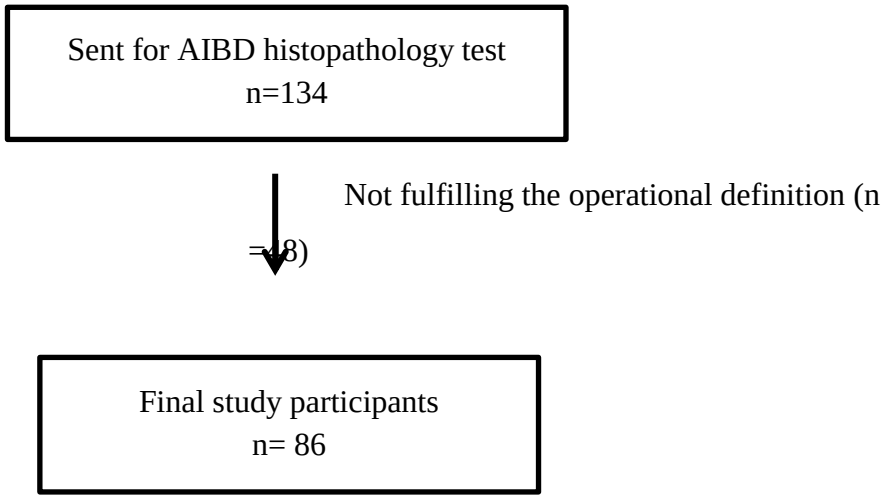

Figure 1: Study participant's flow chart for the study

5.2 Baseline comparison

From the total of 86 study participants, 37.2% (n= 32) of them were male and the rest 62.8% (n= 54) were female, with a mean age of 40.9 year, the minimum age of disease onset being 7 month of age and the maximum age of disease onset was 82 years old. The most frequent year of diagnosis is presented in figure 2.

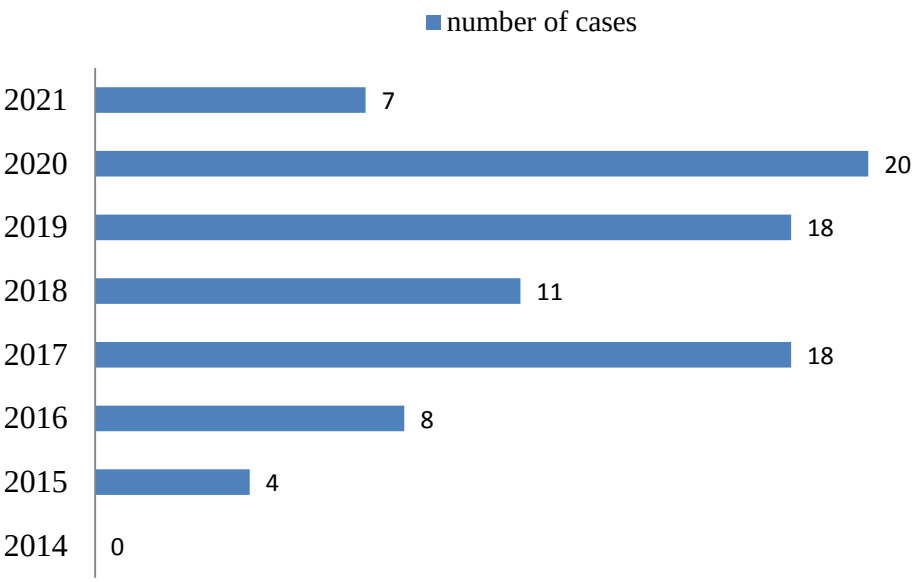

Figure 2: Year of diagnosis with frequency

5.3 Pattern of AIBD

The types of AIBD diagnosed with histopathology result among biopsies sent from January, 2014- June, 2021, at ALERT were 10 in number. Among which the most frequent was Bullous pemphigoid with 34.8% (n=30), followed by pemphigus foliaceus and pemphigus vulgaris each being 24.4% (n=21). Whereas, 4 cases were reported with undistinguished feature of linear IgA dermatosis and/or dermatitis herpetiformis **(Table1)**.

Table 1: Disease spectrum of AIBD from January, 2014- June, 2021

No.	Spectrum of AIBD	Frequency n(%)
1	Bullous Pemphigoid	30 (34.9)
2	Pemphigus Vulgaris	21 (24.4)
3	Pemphigus Foliaceus	21 (24.4)
4	Linear IgA Dermatosis and/or Dermatitis Herpetiformis	4 (4.7)
5	Pemphigus Vegetans	3 (3.5)
6	Linear IgA Dermatosis	2 (2.3)

7	Lichen Planus Pemphigoides	2 (2.3)
8	Pemphigoid Gestationis	1 (1.2)
9	Bullous Lupus Erythematosus	1 (1.2)
10	IgA Pemphigus	1 (1.2)

The most frequently seen AIBD among females were pemphigus vulgaris (n=16) followed by pemphigus foliaceous (n=15). Among male patients the most frequently diagnosed AIBD was bullous pemphigoid (n=17) followed by pemphigus foliaceous (n=6) **(Table 2)**.

Table 2: Frequency of AIBD between Male and female

No.	**Spectrum of AIBD**	**Frequency(n=86)**	
		Male	**Female**
1	Bullous Pemphigoid	17	13
2	Pemphigus Vulgaris	5	16
3	Pemphigus Foliaceous	6	15
4	Linear IgA Dermatosis and/or Dermatitis Herpetiformis	1	3
5	Pemphigus Vegetans	2	1
6	Linear IgA Dermatosis	1	1
7	Lichen Planus Pemphigoides	0	2
8	Pemphigoid Gestationis	0	1
9	Bullous Lupus Erythematosus	0	1
10	IgA Pemphigus	0	1

Bullous pemphigoid was commonly seen above the age of 60years where as it was rare below the age of 20 years.. Both Pemphigus vulgaris and pemphigus foliaceous frequencies were higher at the age group of 20-39 years. An overall frequent AIBD was seen at the age group of 20 -39 years. the age group where least AIBD was seen was below 20 years of age. **(Table 3).**

. **Table 3: Frequency of Spectrum of AIBD by age group**

No.	Spectrum of AIBD	Age frequency(n=86)			
		0-19	20-39	40-59	60-82
1	Bullous pemphigoid	3	5	10	12
2	linear IgA dermatosis	1	1	0	0
3	Pemphigus Vulgaris	3	11	5	2
4	Lichen Planus Pemphigoides	0	1	1	0
5	Pemphigoid Gestationis	0	1	0	0
6	Pemphigus Vegetans	3	0	0	0
7	Pemphigus Foliaceous	3	12	3	3
8	Bullous Lupus Erythematosus	1	0	0	0
9	IgA Pemphigus	0	0	1	0
10	Linear IgA Dermatosis and/or Dermatitis Herpetiformis	1	1	2	0

6. Discussion

A hospital based retrospective cross-sectional study was conducted in which histopathologic reports regarding AIBD elapsing from January, 2014- June, 2021 was obtained from ALERT/ARHI archive in which analysis was done on 86 cases to determine the pattern of AIBD in ALERT hospital.

In this study, the prevalence of BP is the highest (34.9%) followed by PF and PV each being 24.4% among the other types of AIBD. This finding is in coherence with the finding in Europe in which the most common form of AIBD was Bullous pemphigoid with an estimated prevalence of 1/4,000 (4,21). In the contrary to our study;in sudan a 16-years retrospective cross-sectional study was conducted at Khartoum Dermatologic and Veneral Diseases Teaching Hospital to evaluate the epidemiology of autoimmune bullous disease from 2000-2016.585 were included in the study. Pemphigus vulgaris was the most common disease (50.9%),followed by bullous pemphigoid (28.2%). An 11-year retrospective study in Tunisia, Pemphigus was observed to be the most common AIBD (53%), with the majority being PV (61%) (14). In Iran, a 13-year retrospective study was designed to evaluate spectrum of AIBD diseases from documented data obtained from hospitalized patients with AIBDs from October 1999 to October 2012. From 168 patients, 78% had pemphigus (15). In Spain, in a hospital based review study from 2000-2011 found, a total of 61 patients with the following diagnoses and distribution: 36 with PV (59%), 4 with PF (7%),(17). The prevalence of AIBD in calculated based on the ICD-coding-based dataset in Germany revealed about 40,000 AIBD patients including 21,000 patients with BP, 7,700 with PV, and around 2,000 with MMP (23). These differences can be accounted for the difference in study methodology (retrospective versus prospective), the diagnosis modality of AIBD (Immunological versus histological), study set up area (hospital based versus community based), year of assessment(eight years versus other)

In our study from the total of 86 study participants, majority of the AIBD cases were noted in females 62.8% (n= 54) where as it was noted in 37.2% (n= 32) of male. The most frequently seen AIBD among females were pemphigus vulgaris (n=16) followed by pemphigus foliaceous (n=15). Among male patients the most frequently diagnosed AIBD was bullous pemphigoid

(n=17) followed by pemphigus foliaceous (n=6). This finding goes in accordance with the study of Erkan A et al an Europe based study in which overall incidence is slightly higher in females (4). Studies conducted in Finland, in South Africa, in France, in UK support our study finding (12, 18, and 20).

The overall mean age of our study was 40.9 year, the minimum age of disease onset being 7 month of age and the maximum age of disease onset was 82 years old. In our study, Bullous pemphigoid was commonly seen above the age of 60years where as it was rare below the age of 20 years. Both pemphigus vulgaris and pemphigus foliaceous frequencies were higher at the age group of 20-39 years. An overall frequent AIBD was seen at the age group of 20 -39 years. The age group where least AIBD was seen was below 20 years of age. This goes in hand to the findings in Central Europe where BP is typically a disease of the elderly with an estimated median age of onset of after 60 years.(4) In France as well a study showed 92% percent of incident BP cases were aged 70 years or above.(16) In a South Africa study, the mean age of presentation of PV was 48 years with a minimum and maximum age at presentation being 21annd 82 years respectively whereas in PF the mean age was 43 years with a minimum and maximum age at presentation being 12 and 93 years (12). In Taiwan, the mean age of onset of pemphigus was 52.5±15.9 years and people aged 60 years and older had the highest risk of developing pemphigus (5). In Iran, the age of patients at presentation ranged from 1 month to 115 years, with a mean of 47.5±19.93 years (15).

7. Strengths and limitations of the study

Strength

- This study was conducted in one of the country's largest dernatovenerology referral hospital which helps to estimate the magnitude and pattern of AIBD.
- This is the first study conducted in Ethiopia on AIBD, according to the knowledge of the researcher, which can be used as a baseline study for further studies
- This study is based on histopathologic pathology report on AIBD, which is more reliable than mere clinical diagnosis

Limitation

- This study is a retrospective in nature not prospective one, which might limit the number of variables that can be assessed plus decrease the number of study participants due to missed data, since secondary data was used, associations were not able to be constructed.
- Clinical correlations were not taken into account since only histopathological reports were used
- Due to lack of availability the more specific diagnostic modality i.e. immune florescence assay was not used for diagnosis, which might affect the prevalence of AIBD.

8. Conclusion and Recommendations

8.1 Conclusion

This study found that bullous pemphigoid is the most prevalent in the assessed institution site, followed by pemphigus foliaceus and pemphigus vulgaris. The overall mean age of the patients being 40.9 years. Moreover, AIBD was seen in higher predominance in female patients.

8.2 Recommendations

- For researchers who want to pursue their study regarding AIBD, to conduct a prospective large scale(including other hospitals) study with a clinical correlation, to asses in depth and to produce a more need based result, that can be used for policy maker recommendation

- Since AIBD is a chronic illness, it is recommended for researcher to conduct a qualitative study to assess how to improve the quality of life for such patients.

- Moreover, it is recommended to use a confirmatory diagnositic modality of AIBD i.e immunofluorescence study (when available) for further researchers.

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