CLINICAL ETIOLOGY AND HISTOPATHOLOGIC CORRELATION OF EXFOLIATIVE ERYTHRODERMA AT THE KENYATTA NATIONAL HOSPITAL

KAREN WAITHERA WAINAINA

MASTER OF MEDICINE IN DERMATOLOGY

JOMO KENYATTA UNIVERSITY OF AGRICULTURE AND TECHNOLOGY

2026

Clinical Etiology and Histopathologic Correlation of Exfoliative Erythroderma at the Kenyatta National Hospital

Karen Waithera Wainaina

A Thesis Submitted in Partial Fulfillment of the Requirements for the Degree of Master of Medicine in Dermatology of the Jomo Kenyatta University of Agriculture and Technology

2026

DECLARATION

This thesis is my original work and has not been presented for a degree in any other University.

Signature…….Date: ……..

Karen Waithera Wainaina

This thesis has been submitted for examination with our approval as University Supervisors:

Signature…….Date: ……..

Dr. Beatrice Wangari Ndege, MBChB, MMed Internal Medicine, Fellowship Nephrology

JKUAT, Kenya

Signature…….Date: ……..

Dr Priscilla Angwenyi, MBChB, MSc

KNH, Kenya

DEDICATION

I dedicate this work to my parents, Christine and John Wainaina, who have nurtured me with love, kindness, purpose, and unwavering intentionality. Thank you for building a foundation of values that continue to guide me.

ACKNOWLEDGEMENT

I would like to thank God Almighty for opening this door for me.

I cannot appreciate my parents, siblings, and friends enough for the support and grace they have extended my way during this study period.

My gratitude goes to my supervisors, Dr. Wangari Ndege and Dr. Angwenyi, and my mentors, Dr. Kamuri, Dr. Wanyika, and Dr. Kavete for providing guidance as I developed this thesis. Thank you for picking up my calls, replying to my emails and messages, and sparing time for meetings.

I would like to thank the Kenyatta National Hospital community. The patients, study participants, and staff specifically from the Dermatology Unit and Research Department, have been nothing short of gracious.

To my lecturers, fellow postgraduate students, statisticians, and research assistants, thank you for the words of advice and constructive criticism. Thank you, Dr. Zuriel, for your support in facilitating sample analysis.

May God continue to fill your cups and give you satisfaction in all you do.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF APPENDICES

ACRONYMS AND ABBREVIATIONS

BSA	Body Surface Area
CBC	Complete Blood Count
CRP	C - Reactive Protein
ESR	Erythrocyte Sedimentation Rate
HIV	Human Immunodeficiency Virus
ID	Identification Number
KNH/UoN-ERC	Kenyatta National Hospital/University of Nairobi Ethics and Research Committee
KNH	Kenyatta National Hospital
LDH	Lactate Dehydrogenase
NPV	Negative Predictive Value
PPV	Positive Predictive Value
PRP	Pityriasis Rubra Pilaris
SES	Socioeconomic Status
TB	Tuberculosis
WHO	World Health Organization

DEFINITION OF OPERATIONAL TERMS

Clinicopathologic Correlation Agreement between the clinical diagnosis made by a dermatologist and the tissue diagnosis on skin biopsy.

Dermatoses Skin diseases

Exfoliative Erythroderma A dermatologic emergency characterized by diffuse skin redness and scaling involving >70% body surface area. Also known as exfoliative dermatitis or Redman syndrome.

Histopathology Diagnosis following examination of tissues under microscopy, in this case skin biopsies.

ABSTRACT

Exfoliative erythroderma is a dermatologic emergency characterized by diffuse skin redness and scaling involving at least 70% of the body surface area. It is a clinical presentation that usually indicates an underlying primary process. Once a clinical diagnosis of EE was made, prompt supportive measures were instituted while efforts were undertaken to identify the underlying cause of the presentation. These causes were determined clinically and/or through histopathological evaluation following a skin biopsy. Identifying the underlying cause was important for reducing recurrences, complications associated with skin failure, and mortality risk. The correlation between clinical and histopathological diagnoses had not been determined for the Kenyan population. The purpose of the study was to assess the frequency of causes of EE and their histopathologic correlation at Kenyatta National Hospital. This was an ambispective study that included both prospective and retrospective components conducted in the wards and clinics of Kenyatta National Hospital. All adult patients with EE who met the study criteria were included. This study assessed 94 cases of EE at KNH to determine the frequency of skin biopsies and clinicopathologic correlation. Descriptive analysis was used to summarize clinical and pathological findings. Correlation analysis was conducted using Kappa statistics, and sensitivity analysis was also performed to determine the accuracy of clinical findings. A p-value of <0.05 was considered statistically significant at a 95% confidence interval. Data analysis was performed using SPSS version 27. While clinical assessments frequently identified psoriasis and malignancies, the leading histopathologic causes were malignancies (kappa=0.73) and immunobullous diseases (kappa=0.89). To prevent clinical misdiagnosis of the underlying cause of EE, a biopsy-first protocol was recommended for all new EE presentations to ensure diagnostic accuracy and guide next management steps.

CHAPTER ONE

INTRODUCTION

1.1 Background Information

EE (also known as exfoliative dermatitis or Redman syndrome) is a dermatologic emergency in which patients present with diffuse erythema and scaling involving 70% BSA or more (Austad and Athalye, 2023). This clinical presentation represents skin failure characterized by disrupted barrier function, thermal dysregulation, and metabolic instability. Since it represents a clinical manifestation of an underlying primary process, prompt diagnosis of this root cause is essential to reduce morbidity and mortality (Miyashiro and Sanches, 2020).

The diagnostic process begins with supportive care aimed at clinical stabilization. This is followed by a search for etiology (Okoduwa et al., 2009). Drug-induced EE may be identified based on clinical history and physical examination alone (Hoxha et al., 2020). Histopathologic evaluation of skin biopsies is the gold standard for definitive diagnosis (César et al., 2016). These are especially important for distinguishing between benign inflammatory dermatoses and skin malignancies, with reported diagnostic yields between 48-66% (Walsh et al., 1994). Laboratory markers such as elevated inflammatory markers like ESR, anemia, and hypoalbuminemia further assist in assessing and managing systemic impact but remain non-specific for the underlying cause (Deka et al., 2015; El-Hamd et al., 2022).

The causes of EE are broadly categorized into congenital and acquired factors. (César et al., 2016). Congenital causes include ichthyosis in various forms. Acquired causes are more common and include dermatoses where psoriasis and atopic eczema predominate; drug reactions commonly to allopurinol, vancomycin, or carbamazepine; systemic diseases such as Sezary syndrome, a form of cutaneous T cell lymphoma, and solid tumors of lung or gastric origin (Munyao et al., 2007); and idiopathic causes where no clear cause is identified despite extensive workup (Tan et al., 2014; Tso et al., 2021).

Globally, the incidence of EE varies widely, ranging from 0.0355 in outpatient settings to 11.9% in hospitalized patients (Austad and Athalye, 2023). Psoriasis is the leading global etiology, but in the Kenyan landscape, historical data identified eczema as the primary driver at 83%. A high HIV prevalence further complicated the picture as it is strongly associated with severe erythrodermic presentations (Munyao et al., 2007).

Despite the clinical severity, morbidity, and mortality associated with EE, there is a lack of contemporary data regarding clinicopathologic correlation in the Kenyan population. Since the last retrospective study (Munyao et al., 2007), diagnostic protocols and disease patterns have evolved. This study will address this gap in knowledge by determining the frequency of causes at KNH and comparing clinical with histopathologic diagnoses in the same patients to determine the level of accuracy. This will ultimately optimize diagnostic yields and patient outcomes.

1.2 Statement of the Problem

EE, a skin failure syndrome, represents a state where a patient may develop a life-threatening complication such as high-output cardiac failure, dehydration with severe electrolyte imbalances, and/or sepsis. Despite it being a dermatologic emergency, the diagnostic process in KNH is inconsistent. While skin biopsy is the theoretical gold standard to establish the underlying cause, the frequency of utilization of skin biopsies and the diagnostic yields from these biopsies in the Kenyan context are poorly quantified.

The magnitude of the problem lies in the lag in identifying the underlying cause. In the absence of histopathology, patients are often managed empirically for common dermatoses such as psoriasis or atopic eczema, which may mask early cutaneous T cell lymphoma (CTCL). Failure to establish an early accurate diagnosis leads to inappropriate treatment, prolonged hospital stay, recurrences, and increased mortality risk.

This study will identify the specific clinico-pathologic gaps that exist in KNH and determine what value skin biopsies add to patient care in KNH patients with EE.

1.3 Research Question

What is the correlation between the clinical and histopathologic causes of exfoliative erythroderma in adult patients at the Kenyatta National Hospital?

1.4 Study Objectives

1.4.1 Broad Objective

To assess the correlation between the clinical causes of exfoliative erythroderma and their histopathologic diagnoses at Kenyatta National Hospital.

1.4.2 Specific Objectives

1) To determine the clinical causes of exfoliative erythroderma at the Kenyatta National Hospital
2) To determine the frequency of skin biopsies in patients with exfoliative erythroderma at the Kenyatta National Hospital
3) To outline the histopathologic findings of clinically diagnosed exfoliative erythroderma at the Kenyatta National Hospital
4) To assess the correlation between the clinical and histopathologic diagnoses in exfoliative erythroderma at the Kenyatta National Hospital

1.5 Justification of the Study

In skin failure due to EE, delays in identifying the underlying cause lead to poor patient outcomes. The Kenyan clinical patient profile appears to diverge from Western data. Where global literature identifies psoriasis as the leading cause (Cesar et al., 2016), previous local data suggests a much higher prevalence of atopic dermatitis and HIV-associated complications (Munyao et al., 2007). Misdiagnosis of, say, a cutaneous malignancy for a benign dermatosis would lead to inappropriate treatment, prolonged morbidity, and ultimate avoidable mortality. This study is clinically needed as a bridge for an existing gap between clinical suspicion and pathologic certainty to ensure treatment is targeted, effective, and timely.

KNH is the largest teaching and referral hospital in East and Central Africa. This institution serves a high patient volume, diverse population, and complex dermatologic cases. No other hospital in Kenya receives as many dermatology referrals making it best suited as a single study site. While social insurance covers biopsies for all admitted patients in KNH, some bottlenecks exist. These include high laboratory volume loads and reliance on general pathologists instead of specialized dermatopathologists. This can lead to diagnostic delays and non-specific reports. By evaluating current diagnostic yield within this institutional framework, this study identifies how to optimize existing resources to improve diagnostic precision.

This study carries relevance to clinical practitioners by introducing evidence for a "biopsy-first" protocol, encouraging dermatologists managing EE to prioritize histopathology early to maximize diagnostic yield. As the second Kenyan study on EE, and the first to analyze clinicopathologic correlation, these findings will inform national dermatology protocols and assist standardization of exfoliative erythroderma management at tertiary facilities. It also establishes a baseline for future longitudinal studies on treatment outcomes and the role of specialized dermatopathology services in high volume low resource settings. Additionally, it provides a contemporary etiologic profile of EE in the Kenyan setting useful for training residents and medical students to recognize local disease patterns.

This study is innovative in its ambispective approach, capturing both current and historical challenges. By measuring biopsy accuracy, it moves beyond descriptive data to provide a roadmap to reduce diagnostic lag. It ultimately benefits clinicians by clarifying when histopathologic evaluation is non-negotiable, thereby improving overall quality of care in this life-threatening presentation.

CHAPTER TWO

LITERATURE REVIEW

2.1 Introduction

This chapter will review the global and local epidemiology of EE, its complex pathophysiology, its diverse etiologies subcategorized into congenital and acquired, and examine the diagnostic utility of laboratory tests and skin biopsies in managing EE.

2.1.1 Search Strategy

To ensure a comprehensive review, a systemic search was conducted across major online databases including PubMed/MEDLINE, Cochrane Library, Google Scholar, and African Journal Online (AJOL). The key words included in the Medical Subject Heading (MeSH) were “Exfoliative erythroderma” OR “Exfoliative dermatitis”, “Erythroderma AND Kenya”, “Clinicopathologic correlation AND skin biopsy”, “Etiology of erythroderma AND Sub-Saharan Africa”. Any studies published between 1990 and 2024 were included as long as they provided primary data on adult populations, regional etiologic differences, or histopathologic diagnostic yields.

2.2 Epidemiology of Exfoliative Erythroderma

This rare but severe condition has significant geographic variability. Globally, the mean age of onset is between 40-60 years (Akhyani et al., 2005; Pal and Haroon, 1998). It has a consistent male preponderance with cited male:female ratios of 3:2 (Miyashiro and Sanches, 2020). Global estimates put prevalence ranges between 0.035 in outpatient settings to 11.9% in hospitalized dermatologic patients (Austad and Athalye, 2023; Harper-Kirksey, 2018). Kenyan data by Munyao et al. (2007) showed a 13% incidence among dermatologic admissions at KNH. Regional differences show psoriasis leading globally (Amrutha et al., 2021; Razak and Nandakishore, 2017; César et al. 2016). Atopic eczema leads in Kenya (83%) and Togo (Munyao et al., 2007). These differences likely stem from a combination of genetic predispositions, environmental exposures, and varying healthcare access.

2.3 Definition and Clinical Features of Exfoliative Erythroderma

EE is characterized by widespread erythema (skin redness) accompanied by variable scaling of the skin, affecting at least 70% of the body surface area (Harper-Kirksey, 2018).

The diagnostic criteria for exfoliative erythroderma have been consistently outlined in the literature. According to El-Hamd et al. (2022), the primary diagnostic criteria include diffuse erythema and scaling involving >70% of the body surface area. This criterion is essential for distinguishing exfoliative erythroderma from other dermatologic conditions that may present with localized or less extensive skin involvement. Tso et al. (2021) conducted a comprehensive review of the existing literature, analyzing data from multiple studies, and reported similar diagnostic benchmarks. Miyashiro and Sanches (2020) emphasized the need for early recognition and diagnosis based on the extent of skin involvement and characteristic scaling. Their study, conducted in a tertiary care center, involved a retrospective analysis of patient records to identify common diagnostic features and outcomes. The findings reinforced the significance of diffuse erythema and scaling as hallmark features of exfoliative erythroderma.

The clinical presentation of exfoliative erythroderma is marked by a range of symptoms that can significantly impact a patient's quality of life. The primary symptom is the widespread erythema of the skin, which may initially appear as localized reddening of lighter skin or darkening of areas of darker skin, before rapidly progressing to involve a significantly larger body surface area. The erythema is typically accompanied by fine or coarse crusting and scaling, which can be particularly pronounced in areas of skin folds and flexural regions (Austad and Athalye, 2023).

Patients with exfoliative erythroderma also often experience intense pruritus (Albalawi et al., 2024), which can lead to severe discomfort and sleep disturbances. The constant itching may result in excoriations and secondary infections, further complicating the clinical course. In addition to pruritus, patients may report a burning sensation or tenderness of the affected skin (Miyashiro & Sanches, 2020).

Systemic symptoms are also common in exfoliative erythroderma. Fever, chills, and malaise may be present, reflecting the systemic inflammatory response associated with extensive skin involvement (Tso et al., 2021). Lymphadenopathy and hepatosplenomegaly have been reported in some cases, indicating potential systemic involvement beyond the skin (Okoduwa et al., 2009). Dhali et al. (2017) reported anemia, fever, lymphadenopathy, and edema as common signs identified in erythroderma cases.

In a study conducted by Hoxha et al. (2020), the clinical features of exfoliative erythroderma were examined in a cohort of patients presenting to a dermatology clinic. The study design involved a prospective observational methodology, where patients were followed over a period to document the progression of symptoms and response to treatment. The study population included individuals with varying underlying etiologies, providing a comprehensive overview of the clinical spectrum of exfoliative erythroderma.

The findings of Hoxha et al. (2020) highlighted the diverse clinical manifestations of exfoliative erythroderma. In addition to erythema and scaling, patients exhibited edema, particularly in the lower extremities, and nail changes such as onycholysis and subungual hyperkeratosis. These findings underscore the need for a thorough clinical evaluation to identify the full extent of skin and systemic involvement in patients with exfoliative erythroderma.

Moreover, César et al. (2016) conducted detailed clinical examinations and skin biopsies to correlate clinical findings with histopathologic results. The population included patients with both acquired and congenital forms of the condition. The key findings revealed that, in addition to the classic presentation of erythema and scaling, patients with exfoliative erythroderma often experienced significant hair loss (alopecia) and mucosal involvement, including conjunctivitis and cheilitis.

2.4 Pathophysiology of Exfoliative Erythroderma

The pathophysiology is dependent on the underlying cause, but common pathways across various etiologies have been postulated. Complex interactions between

cytokines interleukin (IL) -1, -2, -8, TNF, interferon gamma & ICAM-1 result in increased epidermal cellular division. Shortened epidermal cell transit time and increased mitosis result in cutaneous exfoliation. Incomplete keratinization results from decreased transit time. This may increase the absorption of medications administered transcutaneously through damaged skin (Vearrier, 2021).

2.4.1 Negative Nitrogen Balance

Normal epidermis has a continual turnover of epithelial cells. Cell division occurs in the germinative layer. Maturation follows over approximately 10-12 days. Cells then remain in the stratum corneum for another 12-14 days before being sloughed off.

In exfoliative erythroderma, the number of cells in the basal layer and their mitotic rate is increased. The time cells take to transit through the epidermis is shortened. The exfoliated scales are incompletely keratinized and contain material normally retained by the skin, including proteins, amino acids, and nucleic acids, which may result in a negative nitrogen balance.

2.4.2 Scale and Protein Loss

The amount of scale lost varies by the underlying condition and its severity. Typically, 7.2grams of scale are lost per day when drug reactions underlie exfoliative erythroderma which correlates to 4.2 grams of protein per day. When eczema causes exfoliative erythroderma, 9.6grams of scale correlating with 5.6 grams of protein are lost on average per day. The highest losses are seen with psoriasis where approximately 22.6 grams of scale corresponding to 12.8grams of protein are lost per day. This is as opposed to 0.5 to 1 gram of scale loss per day in normal skin. The result is hypoproteinaemia, reduced oncotic pressure with resultant third spacing of fluid and edema.

2.4.3 Increased Cutaneous Blood Flow

Impaired skin barrier function and increased blood flow to the skin together result in increased transpiration and insensible fluid loss. This causes dehydration. As this

worsens, reflex tachycardia and high-output cardiac failure may occur. Increased heat loss through the skin may lead to compensatory hypermetabolism and cachexia.

2.4.4 Clinical Pointers towards Underlying Etiology

The underlying etiology may be gleaned from a detailed history. It is important to get a complete medical history, including preexisting medical conditions, skin diseases, allergies, and medication used. When obtaining medication history, seek to know not only about prescription medicines, but also about over-the-counter, supplements, and herbal therapies (Cesar et al., 2016). The onset of symptoms is more sudden in exfoliative erythroderma due to drugs, staphylococcal scalded skin syndrome, and leukemia or lymphoma. In children, the onset of symptoms from birth or early life suggests a congenital cause. Worsening with sun exposure suggests certain diagnoses such as lichen planus or pityriasis rubra pilaris (PRP). Patients with PRP frequently have salmon-colored patches with sharply demarcated islands of sparing. Waxy palmoplantar keratoderma, cephalocaudal progression of the disease, and perifollicular keratotic papules are likely to be seen.

Pruritus is a symptom that is very common in patients with exfoliative erythroderma, reportedly affecting 90% of patients (Vearrier, 2021). Pruritus is most severe in patients with atopic dermatitis or Sezary syndrome. Patients with atopic dermatitis will also have a positive personal or family history of atopy, lichenification, prurigo nodules, predominant involvement of flexural skin in adults, and/or cataracts (Vearrier, 2021). Patients with cutaneous T cell lymphoma will also have infiltrated plaques, leonine facies, painful keratoderma with fissuring, and a reddish-purple hue on their lesions.

In addition to the history of use of implicated drugs in drug-induced forms, patients often report no history of prior skin disease, a morbilliform rash preceding their current exfoliation and redness, facial edema, and purpura on dependent sites. Psoriasis is another common cause which may be gleaned from a prior personal or family history, sudden withdrawal of treatment including steroids, presence of inflammatory arthritis, facial sparing, and nail changes such as nail pits, oil spots, and onycholysis (Cesar et al., 2016). The scale in psoriasis is prominent as opposed to the fine scale seen in atopic

dermatitis or dermatophyte infection. In seborrheic dermatitis, a bran-like scale is seen (Vearrier, 2021).

Presence of bullae or crusting points to underlying immunobullous conditions or infections such as bullous impetigo. Cachexia may occur in long-standing erythroderma or where there is an underlying malignancy. Patients with paraneoplastic erythroderma also typically present with hyperpigmentation, fine scale, and a history of malignancy (Vearrier, 2021). Idiopathic erythroderma is common in elderly men, characterized by a relapsing and chronic course, severe pruritus, dermatopathic lymphadenopathy, and palmoplantar keratoderma (Cesar et al., 2016).

2.5 Etiologies of Exfoliative Erythroderma

Exfoliative erythroderma is a multifactorial condition with diverse etiologies that can be broadly categorized into congenital and acquired causes. Acquired causes of exfoliative erythroderma are more common and can be further divided into dermatoses, drug reactions, systemic diseases, and idiopathic causes (Tan et al., 2014; Tso et al., 2021).

2.5.1 Congenital Causes

Congenital ichthyoses are among the primary congenital causes of exfoliative erythroderma. These are a group of genetic disorders characterized by abnormal skin scaling and hyperkeratosis. Congenital ichthyoses can present at birth or shortly thereafter and often persist throughout life. The pathogenesis of congenital ichthyoses involves mutations in genes responsible for skin barrier function, leading to increased skin permeability and susceptibility to environmental triggers (Fischer and Bourrat, 2020).

A study by Oji et al. (2010) provided a comprehensive overview of congenital ichthyoses, describing the clinical manifestations, genetic mutations, and histopathologic features. This multicenter study included patients from dermatology clinics across Europe and utilized genetic testing to identify mutations in key genes such as TGM1, ABCA12, and NIPAL4. The findings highlighted the heterogeneity of

congenital ichthyoses and their significant contribution to cases of exfoliative erythroderma.

2.5.2 Dermatoses

Psoriasis and eczema are the most common dermatoses leading to exfoliative erythroderma. Psoriasis, in particular, is a chronic inflammatory cutaneous disorder characterized by well-demarcated erythematous plaques with overlying thick silvery scales. In some patients, psoriasis can evolve into erythrodermic psoriasis. Psoriatic erythroderma is characterized by extensive erythema and scaling, often accompanied by systemic symptoms such as fever and malaise (Singh et al., 2016). Studies have shown that systemic inflammation in psoriasis involves elevated levels of cytokines like TNF-alpha and IL-17, which play a crucial role in the pathogenesis of erythroderma (Gottlieb et al., 2008).

El-Hamd et al. (2022) analyzed the prevalence of psoriasis as an underlying cause of exfoliative erythroderma. The study involved a retrospective analysis of patient records in a dermatology clinic in Egypt and included histopathologic examination of skin biopsies. The results showed that psoriasis was the leading cause of exfoliative erythroderma, accounting for 40% of cases. This study emphasized the importance of recognizing psoriasis as a potential cause of erythroderma and the need for targeted therapies.

Eczema, particularly atopic dermatitis, is another significant underlying dermatosis. Atopic dermatitis is a chronic inflammatory skin disease characterized by xerosis and intense pruritus. In severe cases, it can lead to erythroderma. Histopathological findings in eczematous erythroderma include spongiosis, acanthosis, and a mixed inflammatory infiltrate. The chronic inflammatory process and skin barrier dysfunction contribute to the systemic spread of the disease (Maheshwari et al., 2018). Munyao et al. (2007) found that atopic eczema was the leading cause of exfoliative erythroderma in Kenya, accounting for 83% of cases. Teclessou et al. (2020), in a study in Togo, documented eczema was almost eightfold more common as a dermatoses leading to erythroderma than psoriasis. Talat et al. (2016) also noted that

eczema was the most common etiological cause, accounting for over a third of erythroderma cases in a tertiary facility in Karachi.

2.5.3 Drug Reactions

Drug reactions are a significant cause of exfoliative erythroderma, with certain medications being more frequently implicated in different regions. Drug-induced exfoliative erythroderma is often a severe hypersensitivity reaction requiring prompt identification and discontinuation of the offending drug. Common histopathological features include interface dermatitis, eosinophilic infiltration, and vacuolar degeneration of the basal layer. Systemic involvement is often indicated by elevated eosinophil counts and liver enzyme abnormalities (Tan et al., 2014).

Hoxha et al. (2020) conducted a prospective observational study in Albania to identify common drugs associated with exfoliative erythroderma. The study included patients presenting to a dermatology clinic over two years and involved detailed patient interviews and clinical evaluations. The findings showed that allopurinol and the anticonvulsant carbamazepine were the main culprits, consistent with reports from other European countries.

In Kenya, Munyao et al. (2007) reported that sulphonamides, penicillin antibiotics, carbamazepine, and acetylsalicylic acid were the leading drugs associated with exfoliative erythroderma. This retrospective study at Kenyatta National Hospital reviewed patient records and highlighted the regional differences in drug-related causes of erythroderma.

A more recent study from Egypt (El-Hamd et al, 2022) found that 9.1% of patients had drug-induced exfoliative erythroderma as confirmed by clinical and histopathological tests. Of these, the most used drugs were diclofenac and captopril. Antibiotics such as penicillin and anticonvulsants such as carbamazepine also featured on the list although not as prominently as in the Kenyan study by Munyao et al (2007). Traditional herbal medicines and Ayurvedic medications have also been explored as potential triggers, with reported frequencies of 1.15% in China (Li J et al, 2012) and 42.8% in India (Itty et al., 2020).

2.5.4 Systemic Diseases

Systemic diseases, particularly malignancies and infections, can also lead to exfoliative erythroderma. Erythroderma can be a paraneoplastic syndrome associated with internal malignancies (Plachouri and Georgiou, 2020), particularly cutaneous T-cell lymphoma (CTCL). Malignancies such as Sezary syndrome and cutaneous T-cell lymphoma are well-known causes of erythroderma (Roccuzzo et al., 2022). Sezary syndrome, an aggressive variant of cutaneous T-cell lymphoma, presents with circulating Sezary cells, erythroderma, and lymphadenopathy.

In CTCL, malignant lymphocytes infiltrate the skin, leading to widespread erythema and scaling. Histopathological examination reveals atypical lymphocytes and epidermotropism, which are hallmark features of CTCL (Gupta et al., 2022). César et al. (2016) revealed that other lymphoproliferative disorders were also significant contributors to exfoliative erythroderma.

In Kenya, Munyao et al. (2007) reported that HIV was the leading systemic disease associated with exfoliative erythroderma, accounting for 20% of cases. This study highlighted the impact of HIV on dermatologic health in sub-Saharan Africa and the importance of integrated care approaches.

Autoimmune diseases such as dermatomyositis and systemic lupus erythematosus (SLE) can also manifest as erythroderma. The histopathophysiological processes involve immune complex deposition, complement activation, and vasculitis. Skin biopsies often show interface dermatitis with lymphocytic infiltration and basal cell degeneration (Sigdha et al., 2017).

Amrutha et al. (2021) found that poor control of other systemic diseases, such as diabetes and hypertension, was the most common cause of relapse. Medication non-adherence came second. This underscores the importance of multidisciplinary integrated patient management, especially in certain conditions such as psoriatic disease.

2.5.5 Idiopathic Causes

Idiopathic exfoliative erythroderma refers to cases where no underlying cause can be identified despite thorough investigations. The prevalence of idiopathic cases varies widely across studies, and can be about 3.9% to 17% in reported studies (César et al., 2016; Miyashiro and Sanches, 2020). Teclessou et al. (2020) in their study in Togo, in fact, recorded that up to 28% of the cases of erythroderma could not be tied to any clinical cause.

The diagnosis of idiopathic exfoliative erythroderma is made by exclusion, requiring comprehensive clinical, laboratory, and histopathologic evaluations to rule out other potential causes. Amrutha et al (2021) report that most of these patients develop CTCL and it is therefore considered a premalignant condition. A few undergo spontaneous remission while others are eventually identified to have an underlying dermatosis following serial skin biopsies every 6 months.

Walsh et al. (1994) conducted a study to investigate the diagnostic accuracy of skin biopsies in exfoliative erythroderma. The study included patients presenting to a dermatology clinic over a five-year period and involved histopathologic examination of skin biopsies. The findings showed that skin biopsies had an accuracy of 48-66% in identifying underlying causes, highlighting the challenges in diagnosing idiopathic cases.

2.6 Diagnosis and Clinical Management of Exfoliative Erythroderma

Exfoliative erythroderma, also known as exfoliative dermatitis or Redman syndrome, is primarily diagnosed based on clinical presentation. The condition is characterized by diffuse erythema and scaling affecting at least 70% of the body surface area, which is a critical diagnostic criterion consistently highlighted in the literature (Sehgal et al., 2004). Pruritus, fever and thickening of skin are clinical signs also commonly identified in most of these patients (Dhali and Haroon, 2017). The clinical diagnosis involves a thorough patient history and physical examination to identify the extent and distribution of skin involvement, as well as associated symptoms such as pruritus, fever, and lymphadenopathy.

Mistry et al. (2015) conducted a comprehensive review of existing studies to establish diagnostic criteria and management models for exfoliative erythroderma. This review included an analysis of research articles from various regions, encompassing diverse patient populations. The study emphasized the importance of recognizing the characteristic diffuse erythema and scaling, which are pivotal in differentiating exfoliative erythroderma from other dermatologic conditions with localized or less extensive skin involvement (Mistry et al., 2015).

Miyashiro and Sanches (2020) further elaborated on the clinical features necessary for the diagnosis of exfoliative erythroderma. Their study, conducted in a tertiary care center, involved a retrospective analysis of patient records to identify common diagnostic features and outcomes. The findings reinforced the significance of diffuse erythema and scaling as hallmark features of exfoliative erythroderma, along with additional symptoms such as intense pruritus, fever, and lymphadenopathy.

2.6.1 Role of Skin Biopsy and Histopathologic Examination

The role of skin biopsy and histopathologic examination in the diagnosis of exfoliative erythroderma is well-documented. Histopathological examination plays a pivotal role in diagnosing erythroderma, though it can be challenging due to overlapping features among different causes. Skin biopsy is particularly important in cases where the underlying cause is not immediately apparent from clinical evaluation alone (Snigdha et al., 2017).

Histopathologic examination can provide valuable insights into the underlying etiology, guiding appropriate management strategies. Spongiosis and acanthosis, sometimes with hyperkeratosis and perivascular infiltrates of eosinophilis, are common in eczematous dermatitis, characterized by epidermal hyperplasia and intercellular edema (Amrutha et al., 2021; Kumar, 2019). Parakeratosis and Munro microabscesses, indicative of psoriasis on histopathological examination, involve retention of nuclei in stratum corneum and presence of neutrophils (Maheshwari et al., 2018). Other signs indicative of psoriasis may include hypogranulosis, suprapapillary thinning, acanthosis and perivascular lymphocytic infiltrates (Amrutha et al., 2021). Atypical lymphocytes and epidermotropism are often seen in erythroderma associated

with cutaneous T-cell lymphoma, as the malignant lymphocytes invade the epidermis (Tan et al., 2014). Perivascular eosinophilic infiltrates, often together with parakeratosis and basal cell vacuolization, on the other hand, are often suggestive of drug-induced erythroderma when a potentially offending agent was recently administered (Amrutha et al., 2021; Gupta et al., 2022).

The key findings of Cesar et al. (2016) indicated that skin biopsies were useful in establishing a diagnosis in 63 out of the 95 patients, resulting in a diagnostic accuracy of 66.3%. The study emphasized the importance of histopathologic examination in identifying specific underlying causes, such as cutaneous T-cell lymphoma, psoriasis, and drug reactions. Walsh et al. (1994), for his part, reported an overall histopathological diagnostic accuracy of 53% in erythroderma.

Amrutha et al. (2021) in their study reported that histopathology conferred a specific dermatosis in only 64.6 % of the skin biopsies. However, the study also noted that the diagnostic accuracy varied depending on the underlying cause, highlighting the need for careful interpretation of biopsy results in conjunction with clinical findings. Other factors that have been noted to improve diagnostic accuracy include biopsy site of a primary lesion and serial skin biopsies, especially to rule out cutaneous T cell lymphoma.

El-Hamd et al. (2022) further investigated the histopathologic features of exfoliative erythroderma in patients in Egypt. This retrospective study involved a detailed review of patient records and histopathologic examination of skin biopsies. The findings revealed that psoriasis was the leading pathologic diagnosis, followed by eczema and drug reactions. The study reported high clinical and histopathologic correlation rates, with a 90.9% correlation for plaque psoriasis and 96.9% for pustular psoriasis. These findings underscore the critical role of skin biopsy in confirming the diagnosis and guiding management. This Egyptian study did not assess interrater variability, or the accuracy of the clinical or histopathologic results. They relied on a percent agreement to determine histopathologic correlation. No study from East Africa has assessed histopathologic correlation so far.

In a study by Miyashiro et al. (2014), clinical features such as pruritus, fever, and lymphadenopathy were correlated with specific histopathological patterns, aiding in the diagnosis of underlying conditions. Zip et al. (1993) revealed that, despite histopathological similarities across different etiologies, specific patterns such as spongiosis in eczema or Munro microabscesses in psoriasis provided crucial diagnostic clues. Diagnosing erythroderma, nonetheless, remains challenging due to the nonspecific nature of the clinical and, in some cases, even the histopathological findings. For instance, nonspecific findings were noted in 43.24% of cases in Gupta et al.'s (2022) study, underscoring the need for repeated biopsies and comprehensive clinical assessments. Repeated biopsies are therefore recommended in cases of inconclusive initial biopsies to capture evolving histopathological changes (Jowkar et al., 2006). Biopsies may fail due to timing if done too early when there is too much inflammatory noise, or too late when the primary lesions have resolved, or a lack of specialized dermatopathology services to review complex cases. Multidisciplinary approaches involving collaboration between dermatologists, pathologists, and other specialists may also increase diagnostic accuracy through a holistic evaluation (Khaled et al., 2010). Serial biopsies, utilizing immunohistochemical staining and molecular diagnostics can also enhance the specificity of histopathological findings, particularly in distinguishing inflammatory from neoplastic conditions (Ram-Wolff et al., 2010).

2.7 Conceptual Framework

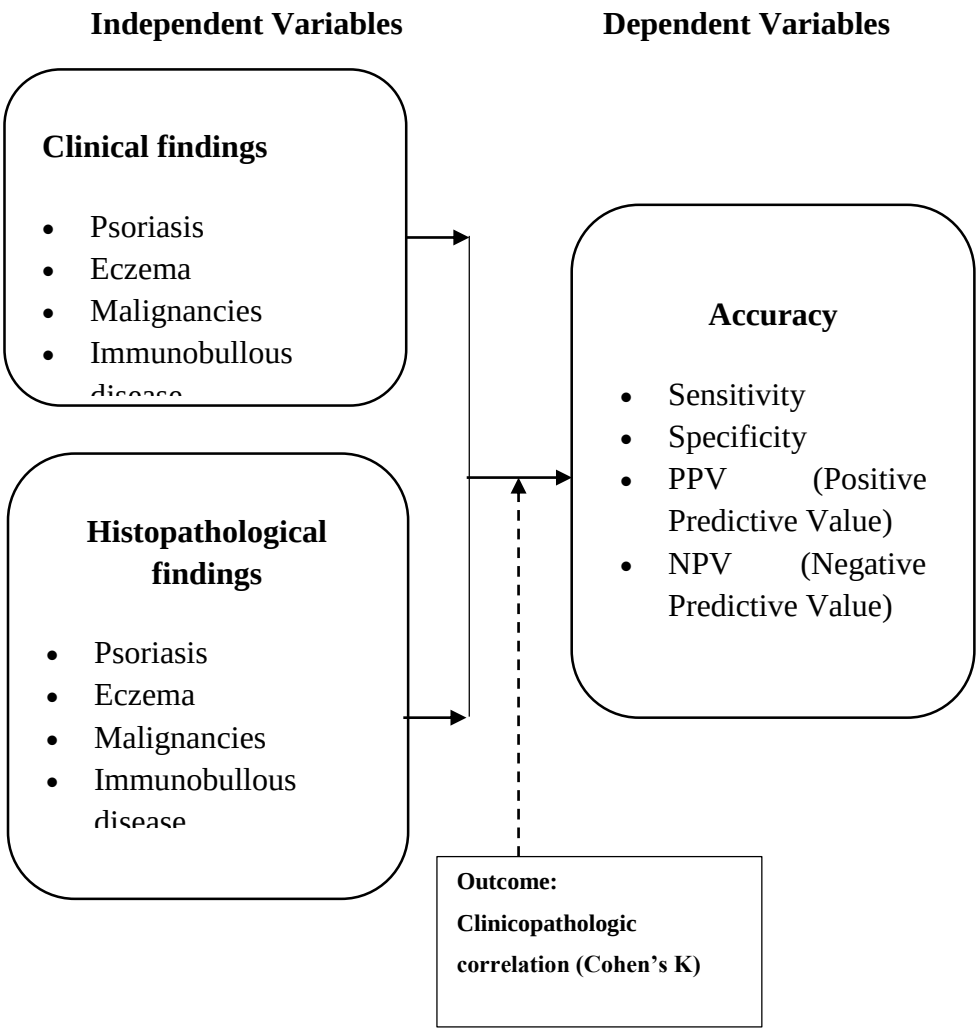


Figure 2.1: Conceptual Framework

CHAPTER THREE

METHODOLOGY

This chapter explained the methods that were used to undertake this study. The chapter described the study setting and population, the study design, study participants and eligibility criteria, ethical review, data collection and data analysis methods that were employed for the research.

3.1 Research Design

This study utilized an ambispective study design. This combined prospective and retrospective approaches. Retrospective data were obtained from the KNH records department from January 2014 to January 2025, noting every patient from the dermatology unit discharged from the ward or managed in the clinics with a diagnosis of exfoliative erythroderma. For the prospective arm, data were obtained from patients seen from February 2025 following a clinical impression of exfoliative erythroderma.

3.2 Study Setting

The Kenyatta National Hospital is the region's largest tertiary referral facility, boasting a bed capacity of 2,400 and a staff of up to 6,000. Located within Nairobi County, the hospital is found in the city's upper hill area. The KNH, a Level 6 facility, serves as a referral center for complex medical problems and specialist treatments at the national and regional levels. Patients are often referred to KNH from other lower-level healthcare facilities across the country. As a Level 6 hospital, KNH is equipped with state-of-the-art facilities and offers a wide range of medical services across various disciplines.

The Department of Medicine at KNH is a key division within the hospital, offering comprehensive healthcare services across several specialized units. Within this department, the Dermatology Unit plays a crucial role in the diagnosis, treatment, and management of patients with various skin conditions. The Dermatology Unit provides care through both inpatient and outpatient services, including specialist clinics that cater to a wide range of dermatological conditions.

Patients for this study were drawn from both the outpatient specialist clinics and the inpatient wards within the Dermatology Unit. The outpatient clinics serve a large number of patients regularly, providing an excellent source of participants for the study. In addition, the inpatient wards house patients with more severe or complex dermatological conditions, offering a diverse patient population for the study.

For the retrospective arm of the study, patient records were obtained from the Health Management Information System (HMIS) at KNH, a comprehensive digital system that maintains detailed records of patient encounters, diagnoses, treatments, and outcomes. These records were utilized to gather historical data on patients who have received care in the Dermatology Unit.

3.3 Study Population

The study population consisted of all patients seen at Kenyatta National Hospital who are confirmed to have skin scaling, exfoliation, and erythema affecting 70% body surface area or more. This included both new and existing patients who meet the inclusion criteria within the study period.

3.3.1 Inclusion Criteria

1. Must have skin scaling, exfoliation, and redness affecting 70% body surface area or more as assessed by the principal investigator.
2. Patients aged 18 years and above.
3. Patients must provide written informed consent to participate in the study (prospective arm)
4. Availability of medical records after getting an approved waiver of consent from ERC.

3.3.2 Exclusion Criteria

1. Patients with cognitive dysfunction since they might struggle to understand the study process, potentially making informed consent challenging.
2. Patients who have incomplete medical records (missing primary diagnosis in retrospective arm).

3.4 Sample Size Determination

The sample size for this study was calculated based on the prevalence of EE as reported in previous studies. Mahajan et al. (2021) reported a clinicopathological correlation of 78.3% among dermatologic admissions at a tertiary facility in India. Using this prevalence rate and aiming for a confidence level of 95% with a margin of error of 5%, the sample size can be determined using the formula for estimating proportions:

$$n_0 = \frac{Z^2 * p(1-p)}{d^2}$$

Where:

n_0 = required sample size
Z = Z-value (1.96 for 95% confidence level)
P = estimated prevalence (0.783)
d = margin of error (0.05)
Therefore n_0 = 260

Using Cochran's formula while modifying for a small population which Munyao et al. (2007) found to be about 146 (N) at the Kenyatta National Hospital (agreeing with historical hospital data), the sample size is calculated as shown:

$$n = \frac{n_0}{1 + \frac{(n_0 - 1)}{N}}$$

$$n = \frac{260}{1 + \frac{(260 - 1)}{146}}$$

Therefore, replacing the values above, the final calculated sample size is 94 patients.

Of these, 4/5 (75 patients) were included in the retrospective arm while 1/5 (19 patients) were included in the prospective arm. This division is justified by the study

duration and data from the records department in KNH which shows that on average, 19 new patients are seen in the dermatology unit with a diagnosis of EE. This is a rare condition making a purely prospective study not feasible given the study timeline.

3.5 Sampling Procedure

The study used a consecutive sampling method, which involves including all eligible patients who present to the dermatology department and are diagnosed with EE during the study period. This method ensures that every patient meeting the inclusion criteria has an equal chance of being included in the study, thereby minimizing selection bias.

For the retrospective analysis, all files meeting the inclusion criteria with an indicated diagnosis of EE were assumed to meet the body surface area requirements, as has been the tradition in the dermatology unit (90%). These files were then assessed for the underlying clinical diagnosis, whether a skin biopsy was performed, and the histopathologic diagnosis

3.5.1 The 70% vs 90% BSA Assumption

To ensure consistency in the two arms, a critical distinction was made:

Prospective participants had real-time BSA assessment by the PI using the Rule of Nines to ensure the 70% threshold was met. For the retrospective arm, the KNH dermatology unit has traditionally used a 90% BSA threshold as the diagnostic benchmark for EE. Based on this institutional precedent, all files labeled EE were assumed to meet the 70% inclusion criteria.

3.5.2 Histopathology and Blinding

To reduce observer bias and misclassification, the following measures were implemented:

Skin biopsies taken from consenting patients in the prospective arms were fixed in 10% neutral buffered formalin and analyzed by the only dermatopathologist in

Nairobi, at Sonar Laboratory. The dermatopathologist was blinded to the initial clinical diagnosis while doing the primary assessment to ensure objectivity.

For the retrospective arm, data was extracted from HMIS system, noting all files with a diagnosis of exfoliative erythroderma or exfoliative dermatitis as per ICD 10 and 11 coding. These files were then manually assessed by the PI and her research assistants noting if biopsies were performed and if they were reported by a general pathologist or a dermatopathologist. The data collection form had data fields to feed this information.

3.6 Recruitment Procedure

Recruitment was conducted by the principal investigator with the help of research assistants. The research assistants underwent thorough training specific to the study's requirements. The training program focused on equipping the research assistants with the skills needed to identify eligible participants, obtain informed consent, and collect data in a manner that ensured accuracy and consistency. The principal investigator and the research assistants had all undertaken Good Clinical Practice Training online and applied these principles during the study. All patients presenting to the dermatology department at Kenyatta National Hospital who had been screened by the principal investigator for symptoms consistent with EE were approached at each respective study area. Eligible patients were approached to participate in the study. The study objectives, procedures, potential risks, and benefits were explained in detail. Written informed consent was obtained from all participants before inclusion in the study. Patients who provided informed consent were enrolled in the study and assigned a unique study identification number for confidentiality and data management purposes. Skin biopsies were then obtained from those who consented to the procedure after the risks and benefits were explained. The cost for outsourcing analysis for these skin biopsies was borne by the study. The patient was educated on wound care and received skin biopsy results at the earliest available opportunity. Any complications from the skin biopsy were documented in real time, and the ethics and research committee was notified within 15 calendar days. Any severe adverse effects, such as severe drug reactions to the local anesthetic, were reported to the ethics and research committee

within 7 calendar days. For the retrospective arm, the principal investigator and the research assistants obtained data from patient records in Kenyatta National Hospital between January 2014 and January 2025 after obtaining a waiver from consent from the ethics and research committee.

3.7 Data Collection Procedure

For the prospective arm, patients attending the outpatient specialist clinics or admitted to the inpatient wards within the Dermatology Unit were screened by the principal investigator and research assistants to identify those who met the inclusion criteria. They calibrated each other's findings to reduce inter rater variability. The clinical diagnosis underlying the patient's EE was also recorded. Relevant clinical data, including demographic information, medical history, and findings from the clinical assessment, were recorded on standardized data collection forms by the research assistants or the principal investigator. The principal investigator then performed skin biopsies on all patients in the prospective arm who consented to the procedure. The samples obtained were fixed in 10% neutral formalin, stored, and transported at room temperature before being sent to the laboratory within 4 days.

The skin biopsies were sent to Sonar Laboratory for assessment by a dermatopathologist. Histology and any special stains, as deemed necessary, were performed. All costs for this outsourced analysis were covered by the study. The skin biopsy findings were recorded and correlated with the clinical diagnosis.

For the retrospective arm, all files with a recorded discharge or admission diagnosis of EE between 2014 and 2025 were assessed by the principal investigator or the research assistants. Demographic data, clinical presentation, and skin examination findings, including body surface area involvement, were obtained from the clinical notes. Body surface area involvement had traditionally been assumed to be 90% in the KNH dermatology unit for EE. Where a particular body surface area had not been recorded but the diagnosis captured was EE, 90% body surface area was assumed to be the case over this 11-year retrospective period. Where skin biopsies had been done, these were recorded and correlated with the clinical diagnosis. For cases where skin biopsies had not been done, the clinical diagnosis was captured, and the file was included in the

analysis to assess the frequency of skin biopsies done for EE in KNH, as well as underlying causes for which skin biopsies were traditionally not done in KNH.

There was no overlap between these two groups of participants. Only new cases were picked for prospective cases. Unique identifiers were placed in the physical patient files for all analyzed files in the retrospective arm to avoid multiple analyses of a single case.

3.8 Procedural steps for prospective patients

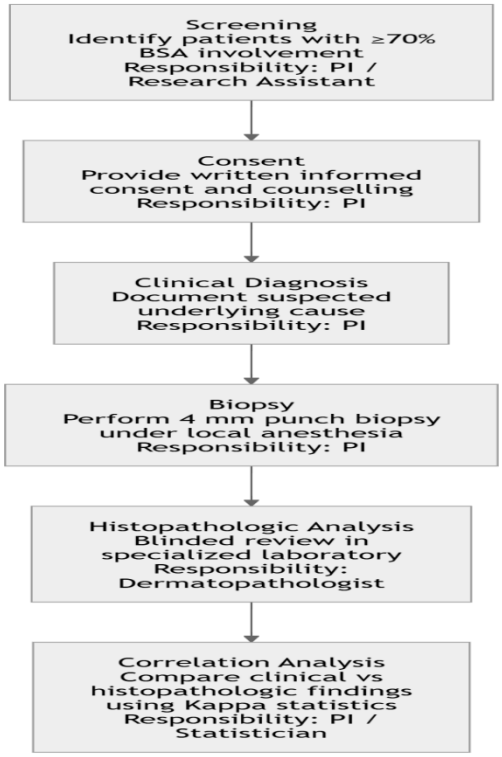


Figure 3.1: Flow Chart Prospective Patients

3.9 Pretesting

A pretest was conducted in the general medical wards in KNH (7^{th} and 8^{th} floor at the time) to determine the clarity and flow of the data collection form for the prospective arm. This avoided testing bias as it was not done in the dermatology unit in KNH.

3.10 Calibration and Bias Control

Calibration exercises were routinely conducted between the PI and research assistants to standardize the clinical assessment of BSA involvement using the rule of nines to reduce inter-rater variability. Standardized medical equipment used included 4mm single use punch devices and rule of nines charts for BSA involvement. The PI oversaw all progressive assessments and performed all skin punch biopsies in the prospective arm to maintain high level clinical rigor.

3.11 Quality Assurance

Ensuring high-quality data was critical for the validity and reliability of this study on exfoliative erythroderma at Kenyatta National Hospital. Several measures were implemented to maintain rigorous quality assurance throughout the study. Firstly, all data collection procedures followed standardized protocols detailed in the study manual. The research assistants recruited for this study were required to have a minimum qualification of a diploma in nursing or clinical medicine qualification or be senior medical students with prior research experience, and therefore knowledgeable in clinical research methodologies and ethical practices. Training sessions were conducted for all research staff to ensure adherence to the research protocols specified for the study. Research staff, including dermatologists, pathologists, and data entry personnel, also underwent comprehensive training to standardize techniques and reduce inter-observer variability.

Regular monitoring visits were conducted by the principal investigator and study coordinators to supervise data collection activities, ensuring compliance with the study protocols and addressing any deviations promptly.

3.12 Data Management and Analysis

3.12.1 Data Cleaning and Entry

Data collected on standardized forms was coded and entered into a secure electronic Microsoft Excel workbook by trained research assistants. During the data entry, cross-verification and identification of discrepancies were performed. A complete case analysis approach was used. Files with missing histopathology results were excluded to maintain the integrity of the correlation analysis. After data entry, a comprehensive data cleaning process, including checking for missing values and outliers, verifying logical consistency (e.g., age consistency with date of birth, lab results within expected ranges), and cross-checking key variables against source documents, was also undertaken to ensure accuracy and consistency. Each of the responses was serialized to ensure that it was accurately entered and could be traced. The collected data were then entered into SPSS version 28 for statistical analysis.

3.12.2 Data Storage and Archival

All paper forms and physical data were stored in locked, secure cabinets accessible only to authorized personnel. Electronic data was stored in a secure, password-protected database. Only the principal investigator, statistician, and study supervisors had access to the data. Different levels of access were assigned based on the role of the staff members, ensuring that only relevant information was accessible according to their responsibilities. Patient identifiers were separated from the main dataset and stored in a secure location. Unique study identification numbers were used in the database to ensure patient anonymity. Regular backups of the electronic database were performed to prevent data loss. Backup files were stored in a separate secure location. Incremental and full backups were scheduled on a daily and weekly basis, respectively. Only the principal investigator had the right to share the study dataset with any other interested party for the purpose of learning and knowledge management. The data was stored for five years, after which the hardcopy papers were shredded, and the soft copy data was stored in the repository.

3.13 Data Analysis

Data was analyzed using both descriptive and inferential analysis. All statistical analyses were performed using the standard SPSS version 27 statistical software package. Categorical data were grouped and analyzed in terms of frequencies and percentages, while continuous variables were assessed using mean and standard deviation. Descriptive statistics were used to summarize the demographic and clinical characteristics of the study population. Measures such as means, medians, standard deviations, and frequencies were reported as appropriate.

The correlation between clinical and histopathologic diagnoses was assessed using kappa statistics. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of histopathologic findings in diagnosing major underlying causes were calculated. The level of significance was set at 0.05. The Kappa statistic was used to determine the level of agreement between clinical and histopathologic diagnoses.

3.14 Ethical Consideration

Before the initiation of the study, Ethical approval was sought from the Kenyatta National Hospital/University of Nairobi Ethics and Research Committee (KNH/UoN-ERC) reference number: P716/09/2024. The study protocol, consent forms, and data collection tools were submitted for review to ensure compliance with ethical standards. A waiver of consent was signed by ERC to access retrospective data from the hospital records department.

Written informed consent was obtained from all participants before any study-related procedures were carried out. The consent process included providing detailed information about the study's purpose, procedures, potential risks and benefits, and the right to withdraw from the study at any time without any consequences to their medical care. Participants were given the opportunity to ask questions and receive clear, understandable answers to ensure they made an informed decision about their participation. Only those who agreed to consent to the study were recruited. Consent obtained also allowed access to patient medical files and registers. A waiver of consent

was approved for retrospective data collection, since the data was de-identified and posed no more than minimal risk to deceased or unreachable patients.

Participant confidentiality, anonymity, and privacy were fully guaranteed and strictly maintained throughout the study period. Personal identifiers were replaced with unique study identification numbers in the dataset to anonymize the data. All electronic data was stored on secure, password-protected systems, and physical data was kept in locked cabinets accessible only to authorized personnel. Results were reported in aggregate form, and no individual participants were identifiable in any publications or presentations resulting from this study. The data obtained were used only for this research and were disseminated solely as findings of the study.

While skin biopsy carries a small risk of bleeding or infection (more than minimal risk), procedures were performed by trained professionals under sterile conditions. The individual histopathological findings from each biopsy were used to inform patient management and were documented in the patients' medical records. Adverse events and complications were closely monitored and promptly addressed. Participants received appropriate medical care for any study-related issues at no cost. Overall, the results were also used by healthcare workers to help improve care for patients with EE. No study costs were personally incurred by any participant in this study. The cost of outsourcing skin biopsy analysis by a dermatopathologist was borne by the study. The tissue blocks obtained will not be used for future studies without seeking the approval of the KNH-UON ERC. No financial guarantees were made, but participants benefited from earlier diagnostic results and expert dermatopathologist review funded by the study. Regardless of the study, they would still have gotten histopathology analysis, most likely by a general pathologist at the hospital, and with results at a later date.

Emotional and psychological support was available via the KNH counseling unit for patients diagnosed with life-threatening malignancies during the study. We also recognized the potential stress of EE, skin biopsies, and waiting for histopathology results for one week. This study was also fully voluntary, and participants were free to withdraw from the study at any point without fear of repercussions.

CHAPTER FOUR

RESULTS

The study sought to assess the correlation between the clinical causes of exfoliative erythroderma and their histopathologic diagnoses at Kenyatta National Hospital. A total of 94 EE patients were recruited into the study, 75 of them retrospectively retrieved from patient records and 19 prospectively obtained through consented patients.

4.1 Characteristics of Exfoliative Erythroderma and Their Histopathologic Correlation at Kenyatta National Hospital

The median age of patients was 45 years, with an interquartile range (IQR) of 30 to 60 years. A higher proportion of males 53(56%) were affected by exfoliative erythroderma. In terms of education level, many patients had secondary education 45(48%), followed by tertiary education 26(28%), and primary education 18(19%). Regarding marital status, 54(57%) of the patients were married. In terms of current occupation, the largest group was unemployed 29(31%), followed by students 18(19%) and farmers 16(17%). The previous occupation data showed that 25(49%) of patients were farmers, 24(47%) had semiskilled or informal jobs as shown in Table 4.1.

Table 4.1: Characteristics of Exfoliative Erythroderma and Their Histopathologic Correlation at Kenyatta National Hospital

Characteristic	**Overall**, n = 94[1]	**Prospective**, n = 19[1]	**Retrospective**, n = 75[1]
Age(years)	**45** (30, 60)	54 (34, 64)	42 (28, 60)
Gender			
Female	41 (44%)	3 (16%)	38 (51%)
Male	**53 (56%)**	16 (84%)	37 (49%)
Education level			
Illiterate	2 (2.2%)	0 (0%)	2 (2.6%)
Not indicated	3 (3.2%)	0 (0%)	3 (4.0%)
Primary	18 (19%)	3 (16%)	15 (20%)
Secondary	**45 (48%)**	9 (47%)	36 (48%)
Tertiary	26 (28%)	7 (37%)	19 (25%)
Marital status			
Married	**54 (57%)**	11 (58%)	43 (57%)
Separated	3 (3.2%)	0 (0%)	3 (4.0%)
Single	25 (27%)	5 (26%)	20 (27%)
Widowed	12 (13%)	3 (16%)	9 (12%)
Current occupation			
Business	8 (8.5%)	3 (16%)	5 (6.7%)
Farmer	16 (17%)	3 (16%)	13 (17%)
Not indicated	1 (1.1%)	0 (0%)	1 (1.3%)
Retired	10 (11%)	1 (5.3%)	9 (12%)
Semis-skilled/informal	8 (8.5%)	4 (21%)	4 (5.3%)
Student	18 (19%)	2 (11%)	16 (21%)
Teacher	4 (4.3%)	2 (11%)	2 (2.7%)
Unemployed	**29 (31%)**	4 (21%)	25 (33%)
Previous occupation			
Farmer	**25 (49%)**	11 (69%)	14 (40%)
Semis-skilled/informal	24 (47%)	5 (31%)	19 (54%)
Teacher	2 (3.9%)	0 (0%)	2 (5.7%)

[1]Median (IQR); n (%)

4.2 Clinical Causes of EE

The study identified diverse clinical causes of EE based on the clinical assessment, as shown in Figure 4.1.

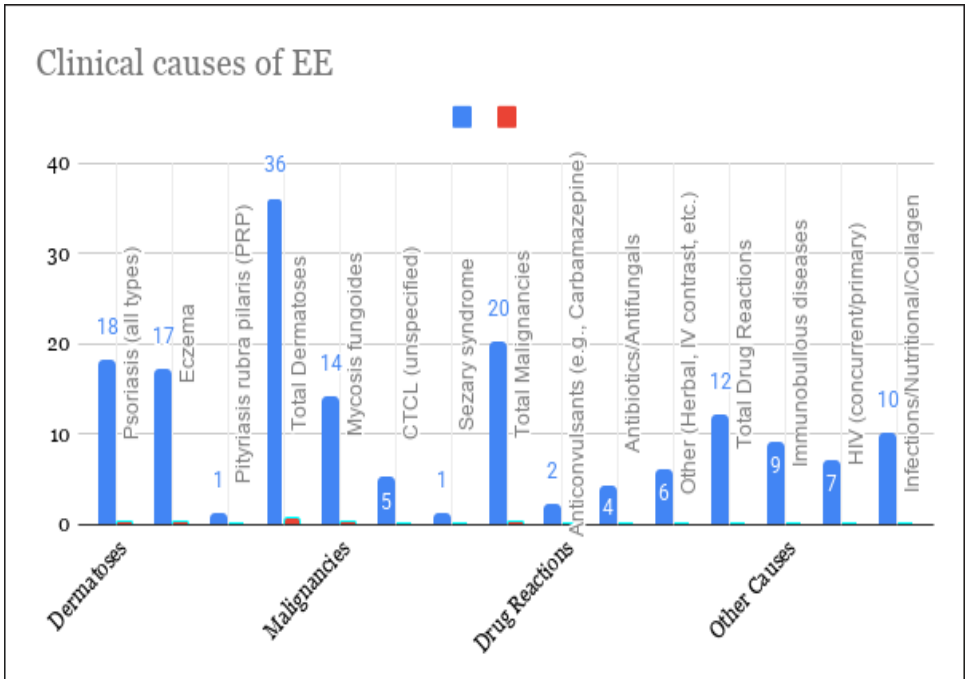


Figure 4.1: Clinical Causes of EE

4.3 Clinical Findings

The common causes of EE included dermatoses (57.45%), with psoriasis 18(24.2%) followed by eczema 17(18.1%). Malignancies 20(21.3%) were the second most common group and the commonest systemic disease, followed by drug reactions 12(12.7%). HIV was present in 7(7.5%) of the cases in our study, as shown in Table 4.2.

Table 4.2: Clinical Causes of EE

Category	Characteristic	Frequency (n)	Percentage (%)
Dermatoses	Psoriasis (all types)	18	24.20%
	Eczema	17	18.10%
	Pityriasis rubra pilaris (PRP)	1	1.10%
	Total Dermatoses	36	57.40%
Malignancies	Mycosis fungoides	14	14.90%
	CTCL (unspecified)	5	5.30%
	Sezary syndrome	1	1.10%
	Total Malignancies	20	21.30%
Drug Reactions	Anticonvulsants (e.g., Carbamazepine)	2	2.10%
	Antibiotics/Antifungals	4	4.30%
	Other (Herbal, IV contrast, etc.)	6	6.40%
	Total Drug Reactions	12	12.70%
Other Causes	Immunobullous diseases	9	9.60%
	HIV (concurrent/primary)	7	7.50%
	Infections/Nutritional/Collagen	10	10.60%
Total		**94**	**100.00%**

*Note: Concurrent HIV, Infections with other clinical causes in some cases

4.4 Frequency of Skin Biopsy

The findings showed that 57(63%) of the patients had a biopsy done, although the frequency was lower in the retrospective arm, 42(57%), compared to the prospective arm of the study, 15(88%).

4.5 Histopathologic Findings of Clinically Diagnosed EE

The findings from histopathological findings revealed that 39.2% were malignancies, followed by psoriasis 25.5%) and immunobullous disease (17.7%), as shown in Table 4.3.

Table 4.3: Histopathologic Findings of Clinically Diagnosed EE

	n	%
Psoriasis	13	**25.49%**
Pustular	3	5.88%
Psoriasis (unspecified)	5	9.80%
Erythrodermic	3	5.88%
Plaque	2	3.92%
Eczema	7	**13.73**%
Pityriasis rubra pilaris	1	**1.96**%
Total dermatoses	34	**41.18%**
Malignancies	20	**39.22%**
Cutaneous T cell (unspecified)	3	5.88%
Sezary syndrome	1	1.96%
Mycosis fungoides	10	19.61%
Non-specific dermatitis	6	**11.76**%
Collagen vascular diseases	1	**1.96**%
Dermatomyositis	1	1.96%
Immunobullous diseases	9	**17.65%**
Bullous pemphigoid	4	7.84%
Pemphigus vulgaris	3	5.88%
Pemphigus foliaceous	2	3.92%
Total	51	100.00%

Note: Multiple biopsies (2 or 3 in 10 cases)

4.5 Correlation between Clinical Findings and Histopathological Findings

4.5.1 Level of Agreement

Table 4.4 presented the level of agreement between clinical diagnoses and histopathologic findings for various skin conditions, as measured by the Kappa statistic and p-value. For psoriasis, the Kappa statistic of 0.43 indicated moderate agreement, with a statistically significant p-value of <0.001. Malignancy showed substantial agreement with a Kappa value of 0.73 and a significant p-value of <0.001. Eczema had a low Kappa value of 0.15, indicating only slight agreement, and the p-value of 0.107 suggests this agreement was not statistically significant. Immunobullous conditions exhibited almost perfect agreement, with a high Kappa statistic of 0.89 and a p-value of <0.001, indicating a statistically significant agreement.

Table 4.4: Level of Agreement

	Kappa statistic	P value
Psoriasis	0.43	<0.001
Malignancy	0.73	<0.001
Eczema	0.15	0.107
Immunobullous	0.89	<0.001

4.5.2 Sensitivity Analysis of Clinical Findings and Histopathological Findings

Table 4.5 showed the accuracy of clinical findings for various skin conditions, with results presented for sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV). For psoriasis, the sensitivity was 64.3% (95% CI: 35.1–87.2). The specificity was high at 86.3% (95% CI: 76.7–92.9), reflecting a strong ability to correctly identify those without psoriasis. The NPV was 93.2% (95% CI: 87.2–96.6), but the PPV was low at 45.0% (95% CI: 2.4–61.6). For malignancy, sensitivity was high at 92.3% (95% CI: 64.0–99.8). Specificity was also high at 92.6% (95% CI: 84.6–97.2. The NPV was very high at 98.7% (95% CI: 91.4–99.8), and the PPV was moderate at 66.7% (95% CI: 47.7–81.4).

For eczema, the sensitivity was low at 37.5% (95% CI: 8.5–75.5). The specificity was good at 84.8% (95% CI: 75.5–91.7), and the NPV was high at 93.6% (95% CI: 89.4–96.2), but the PPV was low at 18.8% (95% CI: 7.6–39.2). Further, for immunobullous conditions, sensitivity was perfect at 100% (95% CI: 66.4–100). Specificity was also high at 97.7% (95% CI: 91.8–99.7), The NPV was 100% (95% CI: 95.7–100), while the PPV was 81.8% (95% CI: 53.4–94.7).

Table 4.5: Accuracy of Clinical Findings

	Sensitivity (95%CI)	Specificity (95%CI)	NPV (95%CI)	PPV (95%CI)
Psoriasis	64.3(35.1, 87.2)	86.3(76.7, 92.9)	93.2(87.2, 96.6)	45.0(2.4, 61.6)
Malignancy	92.3(64.0, 99.8)	92.6(84.6, 97.2)	98.7(91.4, 99.8)	66.7(47.7, 81.4)
Eczema	37.5(8.5, 75.5)	84.8(75.5, 91.7)	93.6(89.4, 96.2)	18.8(7.6, 39.2)
Immunobullous	100(66.4, 100)	97.7(91.8, 99.7)	100(95.7, 100)	81.8(53.4, 94.7)

CHAPTER FIVE

DISCUSSION

5.1 Introduction

This chapter gives detailed analysis and interpretation of study findings in relation to EE knowledge. By synthesizing the sociodemographic profiles, clinical etiologies, and histopathologic correlation data obtained in KNH dermatology unit, this discussion highlights the unique dermatologic landscape in Kenya. The section specifically addresses the diagnostic challenges encountered in a tertiary referral setting and provides a clinical rationale for the proposed "biopsy-first" protocol aimed at improving patient outcomes.

5.2 Sociodemographic Data

The study observed a mean age of onset consistent with global trends, where EE predominantly affects middle-aged and elderly populations (Cesar et al., 2016). The majority of participants fell within the 40–60-year age bracket (Akhayani et al., 2005), a demographic that is statistically more prone to dermatoses such as psoriasis and cutaneous malignancies. The higher incidence in these age groups is often attributed to the long-term progression of pre-existing psoriasis, which may evolve into an erythrodermic state due to systemic triggers, medication withdrawal, or age-related changes in skin physiology (Pal and Haroon, 1998). A notable male preponderance was observed (male-to-female ratio of 3:2), aligning with findings by Munyao et al. (2007) and international studies. This may be linked to higher occupational exposure to environmental risk factors.

5.3 Occupational and Environmental Risk Factors

The patient profiles revealed significant links between occupational exposures and the development of EE. A history of exposure to agrochemicals was identified as a potential risk factor for participants diagnosed with CTCL and Mycosis Fungoides. Chronic exposure to pesticides and fertilizers has been suggested in literature to induce genomic instability in T-lymphocytes, leading to lymphoproliferative disorders

(Olisova at al., 2018). Similarly, certain chemical triggers found in agricultural and industrial settings may act as haptens, initiating the autoimmune response seen in immunobullous conditions like pemphigus foliaceus (Gottlieb et al., 2008). For the cohort with eczematous EE, environmental pollutants and occupational contactants were noted as primary triggers for acute flares. In the Kenyan context, where atopic dermatitis has historically been the leading clinical cause of EE (83%), identifying these external irritants is crucial for long-term management and the prevention of recurrence

5.3.1 The causes of Exfoliative Erythroderma

The current findings revealed that dermatoses were the most common cause of erythroderma (EE), accounting for 57.45%, with psoriasis being the leading cause at 24.2%, followed by eczema at 18.09%. Malignancies contributed to 21.27%, while drug reactions accounted for 12.74%. These findings are consistent with previous studies, including one in India, where psoriasis was identified as the most prevalent pre-existing dermatosis causing erythroderma, found in 45.4% of cases (Amrutha et al., 2021). Likewise, a study in Iran reported that dermatoses were the most common causative factor (59.7%), followed by drug reactions (21.6%), malignancies (11.3%), and idiopathic causes (7.2%) (Akhyani et al., 2005). Both studies used a cross-sectional approach like ours and conducted clinical, laboratory, and biopsy reviews of erythroderma cases, supporting the validity of our findings. This synthesis highlights the consistent identification of dermatoses, particularly psoriasis, as a leading cause of erythroderma across different geographic regions.

These findings align with Munyao et al. (2007), a previous Kenyan study that also identified male predominance (60% males in a 3:2 ratio, compared to 56% males in our study). Munyao et al. found that atopic dermatitis affected 83% of their participants, with HIV being the leading systemic disease in 20% of cases. The differences in findings, particularly the lower prevalence of HIV in our study, may be due to the retrospective nature of Munyao et al.'s analysis, which was conducted over 10 years. Over the years, changes in HIV prevalence and treatment advancements could have influenced the observed trends. Our study and Munyao et al.'s share similar

sociodemographic patterns, but the temporal gap between studies may explain some of the variability, particularly in the frequency of systemic diseases such as HIV.

5.4 The Frequency of Skin Biopsies in Patients with Exfoliative Erythroderma

Our study found that 63% of patients underwent skin biopsies, with a higher rate in the prospective arm (88%) compared to the retrospective arm (57%). Skin biopsies were more frequently performed in new cases (prospective) than in past cases (retrospective). This is comparable to a study in Australia, which reported an 85% higher rate of subsequent biopsies in individuals who had undergone a skin screening examination prior to enrolment (Whiteman et al., 2022). The higher biopsy rate in our study and Whiteman et al.'s study can be attributed to the inclusion of individuals who underwent skin screening, making them more likely to undergo biopsy. In contrast, Sherban et al.'s purely retrospective study had lower biopsy rates, which could be due to the absence of screening and the different study design. The lower biopsy rates in the retrospective arm in the present study was mainly due to lack of documentation in the patient file. Higher rates in the prospective arm were mainly due to follow-up by the researcher, ensuring a higher rate of patients eligible for biopsy, showing that factors such as poor judgement and limited access to equipment may account for the differences in biopsy rates.

5.5 The Histopathologic Findings of Clinically Diagnosed Exfoliative Erythroderma

The current study found that cutaneous T-cell lymphoma was the leading skin biopsy finding, followed by psoriasis (25.49%) and immunobullous diseases (17.65%), with non-specific dermatoses accounting for 11.76%. This is comparable to Jackow et al. (1997), who identified 31 patients with Sezary syndrome and 11 with Mycosis Fungoides (MF), representing 76% of their findings (Jackow et al., 1997). Additionally, our results align with a study in Poland, who reviewed 212 hospitalized cases and found psoriasis as the leading etiology (24%), followed by atopic dermatitis (13.2%) and cutaneous T-cell lymphoma (13.2%), with 19.1% of cases remaining idiopathic (Kliniec et al., 2024). The similarity in findings reflects consistent referral patterns and the use of standardized histopathological protocols at high-volume

tertiary centers. This suggests these studies benefited from similar methodologies and diagnostic frameworks, supporting the reliability of cutaneous T-cell lymphoma as a common diagnosis in these clinical settings.

5.6 The Correlation between the Clinical and Histopathologic Diagnoses in Exfoliative Erythroderma

In our study, the sensitivity of malignancies was 100%, while the lowest sensitivity was observed in immunobullous diseases (55.6%) and eczema (66.7%). Our sensitivity for psoriasis (76.9%) is notably lower than the >90% sensitivity reported in systematic evaluations of structured diagnostic criteria in the UK (Burden-Teh et al., 2018). Similarly, for eczema, our sensitivity of 66.7% is slightly higher than the 62% recorded in patient-reported hand eczema assessments validated against dermatologist diagnoses in Sweden (Svensson et al., 2002). Notably, our study introduces correlation tests, such as Cohen's Kappa, to assess inter-reliability, a method rarely utilized in erythroderma literature. Eczematous dermatitis is often a nonspecific finding in biopsy reports, which may explain the relatively lower sensitivity for eczema. Furthermore, immunobullous diseases require immunofluorescence for definitive diagnosis, which could contribute to the observed lower sensitivity for these conditions. Variations in sensitivity across diseases highlight challenges in diagnostic accuracy and underscore the need for more robust diagnostic protocols for erythroderma.

5.5 Limitations of the Study

Retrospective study design introduced reliance on existing medical records, which vary in completeness and accuracy. Missing data in this arm potentially introduces information bias. Misclassification bias may have occurred in the retrospective arm, where clinical involvement was 70-89% or borderline, but less than 70% may have been erroneously documented as EE. In addition, the study was conducted in a single referral hospital, which may not represent the Kenyan landscape analysis of EE. Thus, there is a risk of missing key pathologies that might have been important to highlight in this study. Conducting a multicenter study would help ensure that many pathologies are identified and guarantee the applicability of the study's findings to the wider Kenyan population.

Further, the low biopsy rate in the retrospective arm was due to lack of comprehensive information on the indication for biopsy or its documentation in the patient file.

CHAPTER SIX

CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

Dermatoses are the leading clinical cause of EE, accounting for over half of the cases, led by psoriasis, then eczema, and followed by systemic diseases. Malignancies are the leading systemic disease-causing EE clinically. The higher biopsy rate in the prospective arm (88 %) versus the retrospective arm (57 %) underscores the importance of active case ascertainment in new presentations. CTCL was the most common biopsy-confirmed diagnosis (39.22 %), which may show late presentation in KNH, given its non-specific nature in some of the early biopsy reports. The diagnostic pathway demonstrated a high correlation between clinical and histopathological findings for immunobullous and malignancy. The low PPV for psoriasis (45.5%) reveals that many inflammatory cases are clinically misdiagnosed. The high sensitivity of histopathology (92.3%) in detecting malignancies confirms that skin biopsy is the essential "gold standard" for differentiating dermatoses from life-threatening cancers.

6.2 Recommendations

These recommendations are primarily addressed to academic researchers, clinicians, dermatologists, and institutional policymakers (KNH-UoN ERC and the Ministry of Health).

Adopt a biopsy-first protocol for all new presentations of exfoliative erythroderma to maximize diagnostic yield.

Establish a multidisciplinary review board comprising dermatologists, pathologists, and immunologists to review complex cases of erythroderma, harmonize clinicopathological correlation, and optimize treatment decisions.

Enhance the HMIS to ensure seamless linking of digital pathology reports with clinical inpatient records to avoid missing data.

Develop and implement institutional or regional clinical guidelines for exfoliative erythroderma that integrate standardized diagnostic algorithms and treatment pathways

Further research areas include a longitudinal approach to follow up idiopathic EE cases, since literature suggests that a significant number develop CTCL; and large multicentre case-control studies to establish the link between agrochemicals and skin diseases in the Kenyan context.

REFERENCES

Akhyani, M., Ghodsi, Z. S., Toosi, S., & Dabbaghian, H. (2005). Erythroderma: a clinical study of 97 cases. *BMC dermatology*, *5*, 1-5. https://doi.org/10.1186/1471-5945-5-5

Albalawi, H. H., Altemani, A. T., Alhweiti, A. S., Alatawi, M. H., Albalawi, A. A., Alharthi, F. S., ... & Algrani, M. S. (2024). Diagnosis and management of erythroderma: a systematic review. *International Journal of Medicine in Developing Countries*, *8*(1), 387-387. https://doi.org/10.24911/IJMDC.51-1700391422

Amrutha, J., Gurram, N. R. N., Pinjala, P., Katakam, B. K., & Thakur, R. S. (2021). A Clinico-Etiological Study of Erythroderma in Adults in a Tertiary Care Centre. *Journal of Evolution of Medical and Dental Sciences*, *10*(37), 3213-3220. https://doi.org/10.14260/jemds/2021/653

Austad, S.S., & Athalye, L., (2023). *Exfoliative Dermatitis*. StatPearls Publishing.

Bolaji, O.-O., Ichechiek, U., (2022). Prevalence, Aetiology and Diagnostic Accuracy for Erythroderma in a Tertiary Centre in Portharcourt, *Nigeria. Am. J. Clin. Med. Res. 10*, 27–31. https://doi.org/10.12691/ajcmr-10-1-6

César, A., Cruz, M., Mota, A., & Azevedo, F., (2016). Erythroderma. A clinical and etiological study of 103 patients. *J. Dermatol. Case Rep. 10*, 1–9. https://doi.org/10.3315/jdcr.2016.1222

Deka, B., Gupta, B., Saha, M., (2015). A Clinico-pathological Study of Erythroderma in a Tertiary Care Centre in Assam, India. *J. Evol. Med. Dent. Sci. 4*, 12133–12142. https://doi.org/10.14260/jemds/2015/1748

Dhali, T.K., & Haroon, M.A., (2017). Exfoliative Dermatitis: A clinico-etiological study. *Int. Arch. Biomed. Clin. Res. 3*. https://doi.org/10.21276/iabcr.2017.3.1.17

di Prinzio, A., Torre, A.C., Cura, M.J., Puga, C., Bastard, D.P., & Mazzuoccolo, L.D., (2022). Adverse Drug Reactions Are the Main Causes of Erythroderma in an Argentinian Teaching Hospital: A Retrospective Study of 70 Patients. *Actas Dermosifiliogr*. *113*, 765–772. https://doi.org/10.1016/j.ad.2022.03.009

El-Hamd, M. A., Ahmed, S. F., Ali, D. G., & Assaf, H. A. E. (2022). Clinicopathological assessment of patients with erythroderma. *Egyptian Journal of Dermatology and Venerology*, *42*(2), 81-91. https://doi.org/10.4103/ejdv.ejdv_32_21

Fischer, J., & Bourrat, E., (2020). Genetics of Inherited Ichthyoses and Related Diseases. *Acta Derm. Venereol. 100,* 5692. Retrieved from https://doi.org/10.2340/00015555-3432

Gottlieb, A. B., Strober, B., Krueger, J. G., Rohane, P., Zeldis, J. B., Hu, C. C., & Kipnis, C. (2008). An open-label, single-arm pilot study in patients with severe plaque-type psoriasis treated with an oral anti-inflammatory agent, apremilast. *Current medical research and opinion*, *24*(5), 1529-1538. https://doi.org/10.1185/030079908X301866

Gupta, P., Das, S., & Roy, A., (2022). A Clinical Study of Patients with Erythroderma Attending a Tertiary Care Hospital in Eastern India. *J. Clin. Diagn. Res*. https://doi.org/10.7860/JCDR/2022/53305.16715

Harper-Kirksey, K., (2018). Erythroderma. Life-Threat. *Rashes* 265–277. https://doi.org/10.1007/978-3-319-75623-3_19

Hoxha, S., Fida, M., Malaj, R., & Vasili, E. (2020). Erythroderma: a manifestation of cutaneous and systemic diseases. *EMJ Allergy Immunol*, 19-00182. https://doi.org/10.33590/emjallergyimmunol/19-00182

Inamadar, A.C., & Ragunatha, S., (2019). The rash that becomes an erythroderma. *Clin. Dermatol. 37*, 88–98. Retrieved from https://doi.org/10.1016/j.clindermatol.2018.12.002

Itty, A., Sridharan, R., Thyvalappil, A., & Sudhamani, B., (2020). Erythroderma: a clinico etiological study of 77 patients in a tertiary care centre in Kerala. *Int. J. Res. Dermatol. 7*, 73. https://doi.org/10.18203/issn.2455-4529.IntJResDermatol20205599

Jowkar, F., Aslani, F.S., & Shafiee, M., (2006). Erythroderma: a clinicopathological study of 102 cases. *J. Pak. Assoc. Dermatol. 16*, 129–133.

Khaled, A., Sellami, A., Fazaa, B., Kharfi, M., Zeglaoui, F., & Kamoun, M., (2010). Acquired erythroderma in adults: a clinical and prognostic study. *J. Eur. Acad. Dermatol. Venereol. 24*, 781–788. https://doi.org/10.1111/j.1468-3083.2009.03526.x

Kumar, R., Huma, S., & Mishra, D. K. (2019). A clinico-etiological study of erythroderma at a tertiary care centre in Jharkhand. *IOSR Journal of Dental and Medical Sciences*, *18*(10), 49-53.

Li, J., & Zheng, H.-Y., (2012). Erythroderma: A Clinical and Prognostic Study. *Dermatology 225*, 154–162. https://doi.org/10.1159/000342365

Mahajan, R., Dogra, S., Bandyopadhyay, M.R., Saikia, U.N., & Kanwar, A.J., (2021). Clinical Patterns and Clinicopathologic Correlation of 100 Patients with Erythroderma in a Tertiary Care Institute in India. *Skinmed 19,* 440–450.

Maheshwari, A., Agarwal, U.S., Meena, R.S., Purohit, S., Thalore, S.K., Nagar, S.G., & Bypass, G., (2018). Clinicopathological correlation in erythroderma 01.

Mistry, N., Gupta, A., Alavi, A., & Sibbald, R., (2015). A Review of the Diagnosis and Management of Erythroderma (Generalized Red Skin). *Adv. Skin Wound Care 28,* 228–36. https://doi.org/10.1097/01.ASW.0000463573.40637.73

Miyashiro, D., Nunes, A., & Sanches, J. A. (2014). Erythroderma: Searching for diagnostic clues in a series of 164 patients.

Miyashiro, D., & Sanches, J.A., (2020). Erythroderma: a prospective study of 309 patients followed for 12 years in a tertiary center. *Sci. Rep. 10,* 9774. https://doi.org/10.1038/s41598-020-66040-7

Munyao, T.M., Abinya, N. a. O., Ndele, J.K., Kitili, P.N., Maimba, J.M., Kamuri, E.N., & Wanyika, H.W., (2007). Exfoliative erythroderma at Kenyatta National Hospital, Nairobi. *East Afr. Med. J. 84,* 566–570. https://doi.org/ 10.4314/eamj.v84i12.9593

Oji, V., Tadini, G., Akiyama, M., Bardon, C. B., Bodemer, C., Bourrat, E., ... & Traupe, H. (2010). Revised nomenclature and classification of inherited ichthyoses: results of the First Ichthyosis Consensus Conference in Sorèze 2009. *Journal of the American Academy of Dermatology*, *63*(4), 607-641. https://doi.org/10.1016/j.jaad.2009.11.020

Okoduwa, C., Lambert, W.C., Schwartz, R.A., Kubeyinje, E., Eitokpah, A., Sinha, S., & Chen, W., (2009). Erythroderma: review of a potentially life-threatening dermatosis. *Indian J. Dermatol. 54,* 1–6. https://doi.org/10.4103/0019-5154.48976

Olisova, O., Zaslavsky, D., Sidikov, A., Chuprov, I., Wenzel, J., & Grekova, E., (2018). Clinical Aspects and Algorithms Diagnostics of Different Types of Erythroderma. *Russ. J. Skin Vener. Dis. 21*, 72–80. https://doi.org/10.18821/ 1560-9588-2018-21-2-72-80

Pal, S., & Haroon, T.S., (1998). Erythroderma: a clinico-etiologic study of 90 cases. *Int. J. Dermatol. 37*, 104–107. https://doi.org/10.1046/j.1365-4362.1998.00228.x

Plachouri, K., & Georgiou, S., (2020). Paraneoplastic erythroderma: an insight on the existing data. *Int. J. Dermatol. 59,* 1429–1436. https://doi.org/10.1111/ ijd.14970

Ram-Wolff, C., Martin-Garcia, N., Bensussan, A., Bagot, M., & Ortonne, N., (2010). Histopathologic diagnosis of lymphomatous versus inflammatory

erythroderma: a morphologic and phenotypic study on 47 skin biopsies. *Am. J. Dermatopathol. 32,* 755–763. https://doi.org/10.1097/DAD.0b013e3181cfbfbf

Razak, A.A., & Nandakishore, B., (2017). A retrospective study of correlation between clinical and histopathological diagnosis in erythroderma. *IOSR J. Dent. Med. Sci. 16,* 60–64.

Roccuzzo, G., Giordano, S., Avallone, G., Rubatto, M., Canonico, S., Funaro, A., …& Quaglino, P., (2022). Sézary Syndrome: Different Erythroderma Morphological Features with Proposal for a Clinical Score System. *Cells 11,* 333. https://doi.org/10.3390/cells11030333

Sehgal, V.N., Srivastava, G., & Sardana, K., (2004). Erythroderma/exfoliative dermatitis: a synopsis. *Int. J. Dermatol. 43,* 39–47. https://doi.org/10.1111/j.1365-4632.2004.01975.x

Singh, R.K., Lee, K.M., Ucmak, D., Brodsky, M., Atanelov, Z., Farahnik, B., …& Liao, W., (2016). Erythrodermic psoriasis: pathophysiology and current treatment perspectives. *Psoriasis Auckl. NZ 6,* 93–104. https://doi.org/10.2147/PTT.S101232

Snigdha, O., George, M., Binitha, M., & Balakrishnan, S., (2017). Clinical profile, etiology and histopathology of patients with erythroderma in South India. *Int. J. Res. Dermatol. 3,* 384. https://doi.org/10.18203/issn.2455-4529.IntJResDermatol20173919

Talat, H., Zehra, U., & Wahid, Z., (2016). A frequency of common etiologies of erythroderma in patients visiting a tertiary care hospital in Karachi. *J. Pak. Assoc. Dermatol. 26,* 48–52.

Tan, G.F.L., Kong, Y.L., Tan, A.S.L., & Tey, H.L., (2014). Causes and features of erythroderma. *Ann. Acad. Med. Singapore 43,* 391–394.

Teclessou, J.N., Akakpo, S.A., & Monsila, G., (2020). Profile of adult erythroderma in hospitals in Lomé (Togo): study of 147 cases. *Our Dermatol. Online 11,* 20–24. https://doi.org/10.7241/ourd.20201.4

Tso, S., Satchwell, F., Moiz, H., Hari, T., Dhariwal, S., Barlow, R., ... & Tso, A. C. Y. (2021). Erythroderma (exfoliative dermatitis). Part 1: underlying causes, clinical presentation, and pathogenesis. *Clinical and Experimental Dermatology*, *46*(6), 1001-1010.https://doi.org/10.1111/ced.14625

Vearrier, D., (2021). *Exfoliative Dermatitis: Practice Essentials, Background, Pathophysiology* Retrieved from https://emedicine.medscape.com/article/762236-overview

Walsh, N.M., Prokopetz, R., Tron, V.A., Sawyer, D.M., Watters, A.K., Murray, S., & Zip, C., (1994). Histopathology in erythroderma: review of a series of cases by multiple observers. *J. Cutan. Pathol. 21,* 419–423. https://doi.org/10.1111/j.1600-0560.1994.tb00283.x

Zip, C., Murray, S., Walsh, N.M.G., (1993). The specificity of histopathology in erythroderma. *J. Cutan. Pathol. 20,* 393–398. https://doi.org/10.1111/j.1600-0560.1993.tb00660.x

APPENDICES

Appendix I: Informed Consent Explanation

PARTICIPANT INFORMATION AND CONSENT FORM.

TITLE OF STUDY: CLINICAL ETIOLOGY AND HISTOPATHOLOGIC CORRELATION OF EXFOLIATIVE ERYTHRODERMA AT THE KENYATTA NATIONAL HOSPITAL

Principal Investigator\and institutional affiliation: Dr. Karen Waithera Wainaina, Kenyatta National Hospital and Jomo Kenyatta University of Agriculture and Technology

Co-Investigators and Institutional Affiliation: Dr Beatrice Wangari Ndege and Dr Priscila Angwenyi, Jomo Kenyatta University of Agriculture and Technology

Introduction

I would like to tell you about a study conducted by the chers listed above. The purpose of this consent form is to give you the information you will need to help you decide whether or not to be a participant in the study. Feel free to ask any questions about the purpose of the research, what happens if you participate in the study, the possible risks and benefits, your rights as a volunteer, and anything else about the research or this form that is not clear. Once we have answered all your questions to your satisfaction, you may decide whether to participate in the study. This process is called 'informed consent'. Once you understand and agree to participate in the study, I will ask you to sign your name on this form. You should understand the general principles that apply to all participants in medical research:

Your decision to participate is entirely voluntary

You may withdraw from the study at any time without necessarily giving a reason for your withdrawal

Refusal to participate in the research will not affect the services you are entitled to in this health facility or other facilities. We will give you a copy of this form for your records.

May I continue? YES / NO

This study has approval by The Kenyatta National Hospital-University of Nairobi Ethics and Research Committee Protocol No. _____

WHAT IS THIS STUDY ABOUT?

This study aims to investigate the causes and characteristics of exfoliative erythroderma, a severe skin condition characterized by widespread redness and peeling of the skin affecting over 70% of the body surface area, in patients at Kenyatta National Hospital. The primary focus is to assess how well the clinical diagnoses made by dermatologists correlate with the findings observed in skin biopsies under a microscope. To achieve this, patients attending the outpatient specialist clinics or admitted to the inpatient wards within the Dermatology Unit will be screened and assessed by dermatology residents or consultants for the presence of exfoliative erythroderma. For those who require a skin biopsy, the procedure will be performed by trained dermatologists to ensure accuracy and safety. The collected skin samples will then be analyzed in a histology laboratory, and the findings will be compared with the initial clinical diagnoses. The ultimate goal is to improve the understanding and management of exfoliative erythroderma at the Kenyatta National Hospital.

There will be approximately **94** participants in this study randomly chosen. We are asking for your consent to consider participating in this study.

WHAT WILL HAPPEN IF YOU DECIDE TO BE IN THIS RESEARCH STUDY?

If you agree to participate in this study, the following things will happen:

You will be interviewed in a private area where you feel comfortable answering questions. This will be done after your clinic visit or when you are admitted to the

ward. The response to the questionnaire will last approximately **30** minutes. The questionnaire will cover topics such as your biodata, history of illness, and treatments you have used.

After the interview guide has been filled completely and correctly, the investigator will take a skin biopsy from you as part of the study's investigations. A skin biopsy is a procedure where a small sample of skin is removed so that doctors can examine it under a microscope. The procedure is usually quick and is done with local anesthesia, so the area where the sample is taken will be numb, and you won't feel much pain. The sample might be taken using a small, sharp blade or a tool that looks like a tiny cookie cutter to remove a small circle of skin. Afterward, the area may be closed with a stitch or two, and a bandage is applied.

We will not contact you after the study is concluded.

ARE THERE ANY RISKS, HARMS DISCOMFORTS ASSOCIATED WITH THIS STUDY?

Medical research has the potential to introduce psychological, social, emotional, and physical risks. Effort should always be put in place to minimize the risks. One potential risk of being in the study is loss of privacy. We will keep everything you tell us as confidentially as possible. We will use a code number to identify you in a password-protected computer database and will keep all of our paper records in a locked file cabinet. However, no system of protecting your confidentiality can be absolutely secure, so it is still possible that someone could find out you were in this study and could find out information about you.

Also, answering questions during the interview may be uncomfortable for you. If there are any questions you do not want to answer, you can skip them. You have the right to refuse to answer any questions asked during the interview.

It may be embarrassing for you to have tests done and personal information collected. We will do everything we can to ensure that this is done in private. Furthermore, all study staff are professionals with special training in these examinations. Also, skin

biopsy procedures may be stressful and painful. The skin biopsy will be done after numbing the site is done.

You may feel some discomfort when we take the biopsy, and you may have a small bruise or swelling in your arm. In case of an injury, illness or complications related to this study, contact the staff at the dermatology ward or clinic right away for sufficient care.

ARE THERE ANY BENEFITS BEING IN THIS STUDY?

You may benefit by receiving tissue sample testing. Also, the information you provide will help us better understand **exfoliative erythroderma**. This information is a contribution to science and **knowledge for clinicians taking care of patients with this condition.**

WILL BEING IN THIS STUDY COST YOU ANYTHING?

It will not cost you anything when you participate in this study.

WILL YOU GET REFUND FOR ANY MONEY SPENT AS PART OF THIS STUDY?

You will be refunded for any costs you may incur as part of your participation in the study. This will not happen regularly as we will strive not to interfere with your usual schedule.

WHAT IF YOU HAVE QUESTIONS IN FUTURE?

If you have further questions or concerns about participating in this study, please call or send a text message to the study staff at the number provided at the bottom of this page.

For more information about your rights as research participant you may contact the Secretary/Chairperson, Kenyatta National Hospital-University of Nairobi Ethics and Research Committee Telephone No. 2726300 Ext. 44102 email uonknh_erc@uonbi.ac.ke.

WHAT ARE YOUR OTHER CHOICES?

Your decision to participate in research is voluntary. You are free to decline participation in the study, and you can withdraw from the study at any time without injustice or loss of any benefits.

STATEMENT OF CONSENT

PARTICIPANT STATEMENT

I have read this consent form or had the information read to me. I have had the chance to discuss this research study with a study counsellor. I have had my questions answered in a language that I understand. The risks and benefits have been explained to me. I understand that my participation in this study is voluntary and that I may choose to withdraw any time. I freely agree to participate in this research study.

I understand that all efforts will be made to keep information regarding my personal identity confidential.

By signing this consent form, I have not given up any of the legal rights that I have as a participant in a research study.

I agree to participate in this research study Yes/No

SAMPLE COLLECTION

I agree to have skin biopsy samples collected as part of this study

Yes/No

SAMPLE STORAGE

I agree to have my specimens preserved for later study

Yes/No

Participant name: _____

Participant signature/Thumb stamp _____ Date _____

Researcher's statement

I, the undersigned, have fully explained the relevant details of this research study to the participant named above and believe that the participant has understood and has willingly and freely given his/her consent.

Researcher's Name: _____ Date: _____
Signature _____

Role in the study: _____

For more information, contact **Dr. Karen Waithera Wainaina** at **0703491344** from January 2025 to December 2025

TAARIFA YA MSHIRIKI NA FOMU YA RIDHAA

KWA AJILI YA KUJISAJILI KATIKA UTAFITI

Kichwa cha Utafiti: Sababu za Kliniki na Uhusiano wa Histopatholojia wa Erythroderma Inayochubua Katika Hospitali ya Kitaifa ya Kenyatta

Mchunguzi Mkuu na Uhusiano wa Taasisi: Dkt. Karen Waithera Wainaina; Hospitali ya Kitaifa ya Kenyatta na Chuo Kikuu cha Kilimo na Teknolojia cha Jomo Kenyatta

Wachunguzi Wenza na Uhusiano wa Taasisi: Dkt Beatrice Wangari Ndege and Dkt Priscila Angwenyi, Chuo Kikuu cha Kilimo na Teknolojia cha Jomo Kenyatta

Utangulizi

Ningependa kukueleza kuhusu utafiti unaofanywa na watafiti waliotajwa hapo juu. Madhumuni ya fomu hii ya ridhaa ni kukupa taarifa utakazohitaji ili kukusaidia kuamua kama unataka kushiriki katika utafiti huu au la. Jisikie huru kuuliza maswali yoyote kuhusu madhumuni ya utafiti, nini kitatokea ukishiriki, hatari na faida

zinazowezekana, haki zako kama mshiriki wa kujitolea, na chochote kingine kuhusu utafiti huu au fomu hii ambacho haujaelewa. Tukishajibu maswali yako yote kwa kuridhika, unaweza kuamua kushiriki au kutoshiriki katika utafiti huu. Mchakato huu unaitwa 'ridhaa iliyofahamishwa'. Ukishaelewa na kukubali kushiriki katika utafiti huu, nitaomba usaini jina lako kwenye fomu hii. Unapaswa kuelewa kanuni za jumla zinazotumika kwa washiriki wote wa utafiti wa matibabu:

Uamuzi wako wa kushiriki ni wa hiari kabisa.

Unaweza kujiondoa kutoka katika utafiti wakati wowote bila kutoa sababu yoyote ya kujiondoa kwako.

Kukataa kushiriki katika utafiti hakutaathiri huduma unazostahili katika kituo hiki cha afya au vituo vingine.

Tutakupa nakala ya fomu hii kwa kumbukumbu zako. Je, naweza kuendelea? NDIYO / HAPANA

Utafiti huu umepata idhini ya Kamati ya Maadili na Utafiti ya Hospitali ya Kitaifa ya Kenyatta-Chuo Kikuu cha Nairobi Protokali Na. _____

UTAFITI HUU UNAHUSU NINI?

Utafiti huu unalenga kuchunguza sababu na sifa za ugonjwa wa ngozi wa exfoliative erythroderma, hali kali ya ngozi inayojulikana kwa uwekundu mwingi na kumenyuka kwa ngozi ikihusisha zaidi ya asilimia 70 ya eneo la mwili, kwa wagonjwa katika Hospitali ya Kitaifa ya Kenyatta. Lengo kuu ni kutathmini jinsi utambuzi wa kliniki uliofanywa na madaktari wa ngozi unavyolingana na matokeo yaliyopatikana kwenye vipimo vya biopsy ya ngozi chini ya hadubini. Ili kufanikisha hili, wagonjwa wanaohudhuria kliniki maalum za wagonjwa wa nje au waliolazwa katika wadi za Kitengo cha Dermatology watapimwa na kutathminiwa na wakazi wa dermatology au washauri kwa uwepo wa exfoliative erythroderma. Kwa wale wanaohitaji biopsy ya ngozi, utaratibu utafanywa na madaktari wa ngozi waliofunzwa ili kuhakikisha usahihi na usalama. Sampuli za ngozi zilizokusanywa zitachambuliwa katika maabara ya histolojia, na matokeo yatalinganishwa na utambuzi wa awali wa kliniki. Lengo kuu

ni kuboresha uelewa na usimamizi wa exfoliative erythroderma katika Hospitali ya Kitaifa ya Kenyatta. Kutakuwa na washiriki takriban 94 katika utafiti huu waliochaguliwa kiholela. Tunaomba ridhaa yako ili kushiriki katika utafiti huu.

NINI KITATOKEA UKIAMUA KUSHIRIKI KATIKA UTAFITI HUU?

Ukiamua kushiriki katika utafiti huu, mambo yafuatayo yatatokea:

Utahojiwa katika eneo la faragha ambapo utajisikia huru kujibu maswali. Hii itafanyika baada ya ziara yako ya kliniki au wakati umelazwa wodini. Kujibu dodoso kutachukua takriban dakika 30. Dodoso litahusu mada kama vile taarifa zako binafsi, historia ya ugonjwa na matibabu uliyotumia.

Baada ya mwongozo wa mahojiano kujazwa kikamilifu na kwa usahihi, mchunguzi na msaidizi wake watachukua sampuli ya ngozi kutoka kwako kama sehemu ya uchunguzi wa utafiti.

Hatutawasiliana nawe baada ya utafiti kukamilika.

JE, KUNA HATARI, MADHARA AU USUMBUFU WOWOTE UNAOHUSISHWA NA UTAFITI HUU?

Utafiti wa matibabu una uwezo wa kuleta hatari za kisaikolojia, kijamii, kihisia na kimwili. Jitihada zinafaa kuwekwa ili kupunguza hatari hizi. Hatari moja inayoweza kutokea kwa kushiriki katika utafiti huu ni kupoteza faragha. Tutahifadhi kila kitu utakachotuambia kuwa siri kadri inavyowezekana. Tutatumia namba ya siri kukutambua kwenye hifadhidata ya kompyuta yenye ulinzi wa nenosiri na tutahifadhi rekodi zote za karatasi kwenye kabati lililofungwa kwa ufunguo. Hata hivyo, hakuna mfumo wa kulinda usiri wako ambao unaweza kuwa salama kabisa, kwa hivyo bado kuna uwezekano kwamba mtu anaweza kugundua ulikuwa katika utafiti huu na kugundua habari kuhusu wewe. Pia, kujibu maswali wakati wa mahojiano kunaweza kukufanya ujisikie vibaya. Kama kuna maswali yoyote ambayo hutaki kujibu, unaweza kuyaacha. Una haki ya kukataa kujibu maswali yoyote yaliyo ulizwa wakati wa mahojiano. Inawezekana ukaona aibu wakati wa vipimo na ukusanyaji wa taarifa binafsi. Tutafanya kila tuwezalo kuhakikisha kuwa hili linafanyika kwa faragha. Zaidi

ya hayo, wafanyakazi wote wa utafiti ni wataalamu walio na mafunzo maalum katika uchunguzi huu. Pia, taratibu za biopsi ya ngozi zinaweza kuwa za kusisitisha na za maumivu. Biopsi ya ngozi itafanywa baada ya ganzi kufanyika kwenye eneo husika. Unaweza kujisikia usumbufu kidogo wakati wa kuchukua biopsi na unaweza kuwa na alama ndogo au uvimbe kwenye mkono wako. Iwapo utapata jeraha, ugonjwa au matatizo yanayohusiana na utafiti huu, wasiliana na wafanyakazi wa wodi ya dermatology au kliniki mara moja kwa ajili ya matibabu yanayofaa.

JE, KUNA FAIDA YOYOTE YA KUWA KATIKA UTAFITI HUU?

Unaweza kufaidika kwa kupokea vipimo vya sampuli za tishu bure. Pia, taarifa utakazotoa zitatusaidia kuelewa vizuri zaidi erythroderma inayochubua. Taarifa hizi ni mchango kwa sayansi na kwa maarifa kwa wataalamu wanaowatunza wagonjwa wenye hali hii.

JE, KUSHIRIKI KATIKA UTAFITI HUU ITAKUGHARIMU CHOCHOTE?

Haitakugharimu chochote kushiriki katika utafiti huu.

JE, UTARUDISHIWA PESA ZOZOTE UTAKAZOTUMIA KAMA SEHEMU YA UTAFITI HUU?

Utarudishiwa gharama yoyote utakayopata kama sehemu ya kushiriki kwako katika utafiti. Hili halitatokea mara kwa mara kwani tutajitahidi kutokuingilia ratiba yako ya kawaida.

NINI KAMA UTAPATA MASWALI KATIKA SIKU ZA USONI?

Iwapo utapata maswali zaidi au wasiwasi kuhusu kushiriki katika utafiti huu, tafadhali piga simu au tuma ujumbe wa maandishi kwa wafanyakazi wa utafiti kwa namba itakayopatikana chini ya ukurasa huu. Kwa taarifa zaidi kuhusu haki zako kama mshiriki wa utafiti, unaweza kuwasiliana na Katibu/Mwenyekiti, Kamati ya Maadili na Utafiti ya Hospitali ya Kitaifa ya Kenyatta-Chuo Kikuu cha Nairobi kwa simu namba 2726300 Ext. 44102 au barua pepe uonknh_erc@uonbi.ac.ke.

NINI CHAGUO ZAKO NYINGINE?

Uamuzi wako wa kushiriki katika utafiti ni wa hiari. Unaruhusiwa kukataa kushiriki katika utafiti huu na unaweza kujiondoa wakati wowote bila dhuluma au kupoteza manufaa yoyote.

KUSHIRIKI KATIKA UTAFITI, UKUSANYAJI WA SAMPULI, NA UHIFADHI WA SAMPU

KUSHIRIKI KATIKA UTAFITI (TAMKO LA RIDHAA)

Nimesoma fomu hii ya ridhaa au nimeelezwa taarifa hizi. Nimepata nafasi ya kujadili utafiti huu na mshauri wa utafiti. Maswali yangu yamejibiwa kwa lugha ninayoelewa. Hatari na faida zimeelezwa kwangu. Ninaelewa kuwa kushiriki kwangu katika utafiti huu ni hiari na kwamba ninaweza kujiondoa wakati wowote. Nakubali kwa hiari kushiriki katika utafiti huu wa kisayansi. Ninaelewa kuwa juhudi zote zitafanywa ili kuweka taarifa zinazohusu utambulisho wangu binafsi kuwa siri. Kwa kusaini fomu hii ya ridhaa, sijatoa haki zozote za kisheria nilizonazo kama mshiriki wa utafiti.

Nakubali kushiriki katika utafiti huu Ndio/Hapana

UKUSANYAJI WA SAMPULI

Nakubali kukusanywa kwa sampuli za biopsi ya ngozi kama sehemu ya utafiti huu. Ndiyo / Hapana

UHIFADHI WA SAMPULI

Nakubali kuhifadhiwa kwa sampuli zangu kwa ajili ya utafiti wa baadaye. Ndiyo / Hapana

Jina la mshiriki: _____ Sahihi ya mshiriki/Mhuri wa kidole

Tarehe _____

Tamko la Mtafiti

Mimi, aliyejibainisha hapa chini, nimeeleza kikamilifu maelezo muhimu ya utafiti huu kwa mshiriki aliyebainishwa hapo juu na naamini kwamba mshiriki ameielewa na amepewa ridhaa kwa hiari.

Jina la Mtafiti: _____

Tarehe: _____ Sahihi _____

Jukumu katika utafiti: _____

Kwa taarifa zaidi, wasiliana na **Dr. Karen Waithera Wainaina** kwa **0703491344** kutoka Januari 2025 hadi Disemba 2025

Appendix II: Data Collection Tool

Sociodemographic data	
Identifier	
Age	
Gender	
Level of education	
Marital status	
Residence: location	
County	
Occupation: Current	
Previous: list all	

Skin biopsy ☐ Done ☐ Not done.

Reported findings if done ……

……..……

……..……

Conclusion……

……...……

…….

Clinical diagnosis: Exfoliative erythroderma secondary to

CLINICAL DIAGNOSIS	**TICK AS APPROPRIATE**	**ADDITIONAL INFORMATION**
Psoriasis		
Atopic dermatitis		
Drug reaction		
Immunobullous disease		
Cutaneous T cell lymphoma		
Others		

Multiple biopsies

YES NO

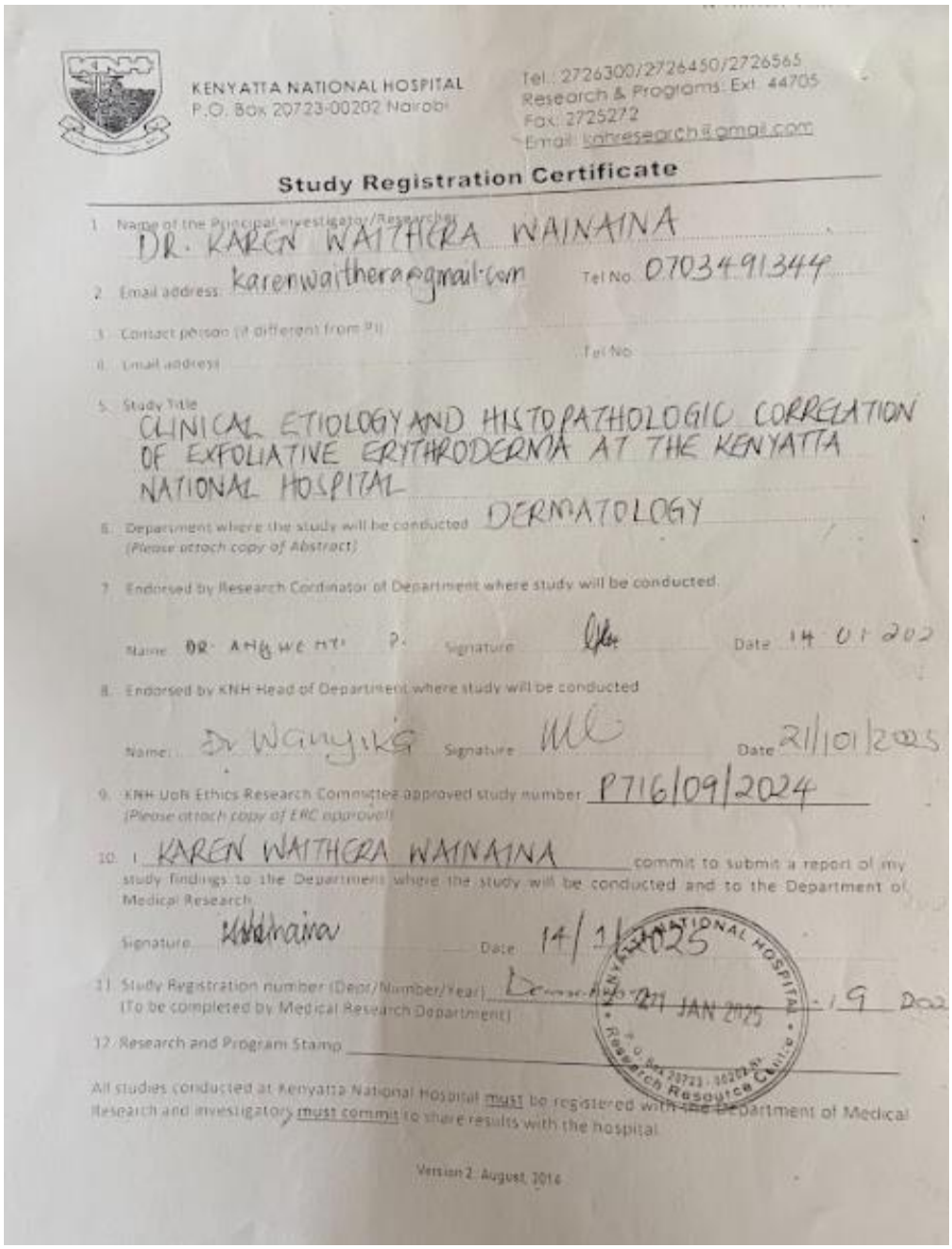
If Yes, indicate findings from each biopsy and date each was done

……

……

If biopsy reported by consultant dermatopathologist, kindly indicate alongside biopsy findings.

Appendix III: Research Approvals



KENYATTA NATIONAL HOSPITAL
P.O. Box 20723-00202 Nairobi

Tel: 2726300/2726450/2726565
Research & Programs: Ext 44705
Fax: 2725272
Email: knhresearch@gmail.com

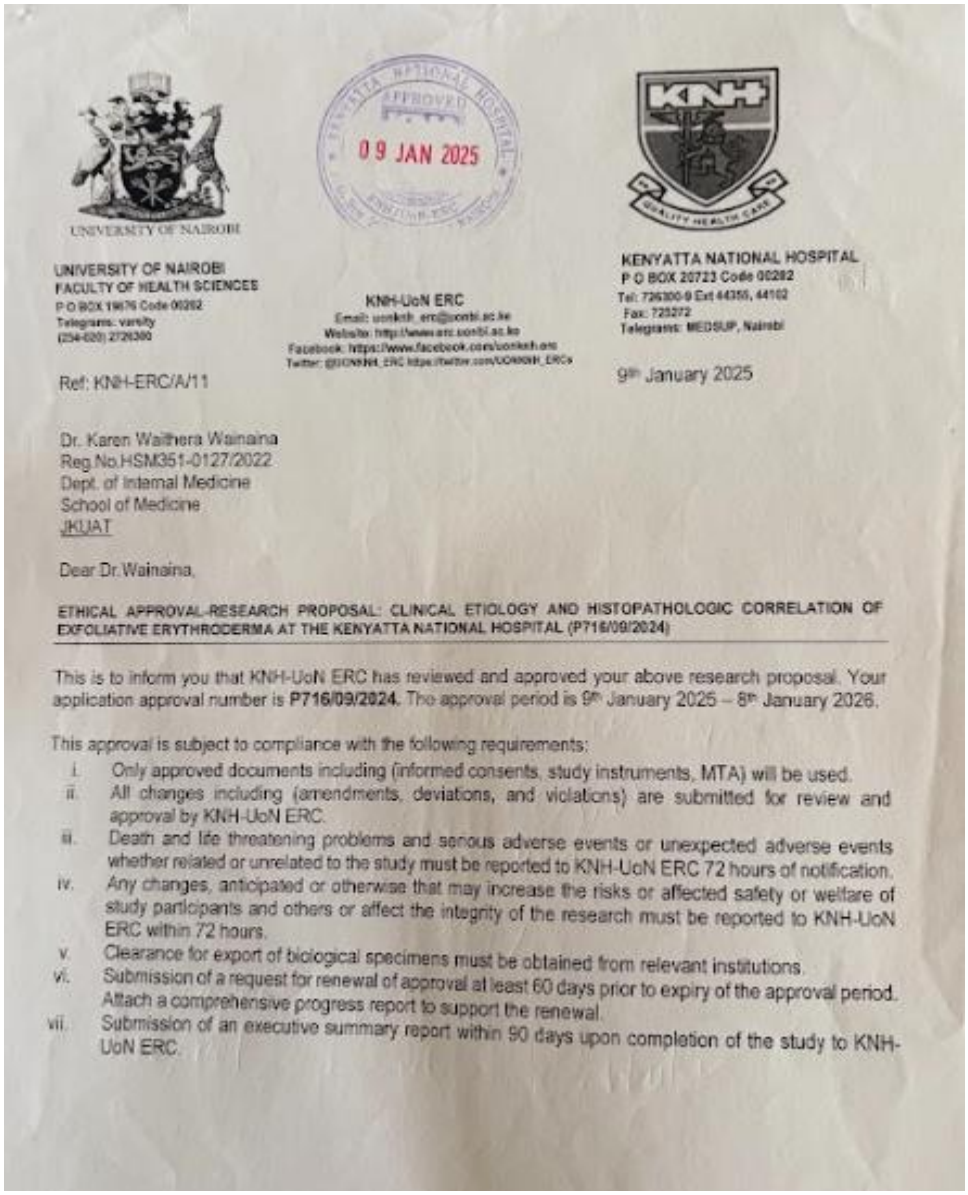
Study Registration Certificate

1. Name of the Principal Investigator/Researcher: DR. KAREN WAITHERA WAINAINA
2. Email address: karenwaithera@gmail.com Tel No. 0703491344
3. Contact person (if different from PI):
4. Email address: Tel No:
5. Study Title: CLINICAL ETIOLOGY AND HISTOPATHOLOGIC CORRELATION OF EXFOLIATIVE ERYTHRODERMA AT THE KENYATTA NATIONAL HOSPITAL
6. Department where the study will be conducted: DERMATOLOGY
   (Please attach copy of Abstract)
7. Endorsed by Research Coordinator of Department where study will be conducted.
   Name: DR. AMBWENI P. Signature: Date: 14/01/202
8. Endorsed by KNH Head of Department where study will be conducted
   Name: Dr Wanyiki Signature: Date: 21/01/2025
9. KNH UoN Ethics Research Committee approved study number: P716/09/2024
   (Please attach copy of ERC approval)
10. I KAREN WAITHERA WAINAINA commit to submit a report of my study findings to the Department where the study will be conducted and to the Department of Medical Research
    Signature: Date: 14/1/2025
11. Study Registration number (Dept/Number/Year): Derm/[illegible]/27 JAN 2025 /19 202
    (To be completed by Medical Research Department)
12. Research and Program Stamp

KENYATTA NATIONAL HOSPITAL • Research Resource Centre • P.O. Box 20723-00202 Nairobi

All studies conducted at Kenyatta National Hospital must be registered with the Department of Medical Research and investigators must commit to share results with the hospital.

Version 2: August, 2016



UNIVERSITY OF NAIROBI

APPROVED
09 JAN 2025

KENYATTA NATIONAL HOSPITAL

UNIVERSITY OF NAIROBI
FACULTY OF HEALTH SCIENCES
P O BOX 19676 Code 00202
Telegrams: varsity
(254-020) 2726300

KNH-UoN ERC
Email: uonknh_erc@uonbi.ac.ke
Website: http://www.erc.uonbi.ac.ke
Facebook: https://www.facebook.com/uonknh.erc
Twitter: @UONKNH_ERC https://twitter.com/UONKNH_ERC1

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9 Ext 44355, 44102
Fax: 725272
Telegrams: MEDSUP, Nairobi

Ref: KNH-ERC/A/11

9th January 2025

Dr. Karen Waithera Wainaina
Reg.No.HSM351-0127/2022
Dept. of Internal Medicine
School of Medicine
JKUAT

Dear Dr.Wainaina,

ETHICAL APPROVAL-RESEARCH PROPOSAL: CLINICAL ETIOLOGY AND HISTOPATHOLOGIC CORRELATION OF EXFOLIATIVE ERYTHRODERMA AT THE KENYATTA NATIONAL HOSPITAL (P716/09/2024)

This is to inform you that KNH-UoN ERC has reviewed and approved your above research proposal. Your application approval number is **P716/09/2024.** The approval period is 9th January 2025 – 8th January 2026.

This approval is subject to compliance with the following requirements:

i. Only approved documents including (informed consents, study instruments, MTA) will be used.
ii. All changes including (amendments, deviations, and violations) are submitted for review and approval by KNH-UoN ERC.
iii. Death and life threatening problems and serious adverse events or unexpected adverse events whether related or unrelated to the study must be reported to KNH-UoN ERC 72 hours of notification.
iv. Any changes, anticipated or otherwise that may increase the risks or affected safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH-UoN ERC within 72 hours.
v. Clearance for export of biological specimens must be obtained from relevant institutions.
vi. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. Attach a comprehensive progress report to support the renewal.
vii. Submission of an executive summary report within 90 days upon completion of the study to KNH-UoN ERC.

REPUBLIC OF KENYA

NATIONAL COMMISSION FOR
SCIENCE,TECHNOLOGY & INNOVATION

Ref No: **949031**

Date of Issue: **21/January/2025**

RESEARCH LICENSE

This is to Certify that Dr.. Karen Waithera Waisaina of Jomo Kenyatta University of Agriculture and Technology, has been licensed to conduct research as per the provision of the Science, Technology and Innovation Act. 2013 (Rev.2014) in Nairobi on the topic: Clinical Etiology and Histopathologic Correlation of Exfoliative Erythroderma at Kenyatta National Hospital for the period ending : 21/January/2026.

License No: **NACOSTI/P/25/415341**

949031

Applicant Identification Number

Director General
NATIONAL COMMISSION FOR
SCIENCE,TECHNOLOGY &
INNOVATION

Verification QR Code

NOTE: This is a computer generated License. To verify the authenticity of this document,
Scan the QR Code using QR scanner application.

See overleaf for conditions

KENYATTA NATIONAL HOSPITAL
P.O. BOX 20723, 00202 Nairobi

Tel.: 2726300/2726450/2726550
Fax: 2725272
Email: knhadmin@knh.or.ke

Ref: KNH/HOD-MED/31/VOL.II **Date: 15th January 2025**

Dr. Karen Waithera
Reg. No. HSM351-0130/2022
Dept. of Internal Medicine
School of Medicine
J.K.U.A.T.

Dear Karen

RE: APPROVAL TO CONDUCT A STUDY AT THE KNH MEDICINE DEPARTMENT - DERMATOLOGY UNIT

Following approval by the KNH/UON-Ethics & Research Committee for your research proposal and subsequent filing of the study registration certificate, this is to inform you that authority has been granted to collect data in Medicine Department, on your study titled "**Clinical etiology and histopathologic correlation of exfoliative erythroderma at Kenyatta National Hospital Kenya**".

By a copy of this letter, **ACN - MOPC/ POPC** is informed and requested to facilitate.

You will also be required to submit a report of your study findings to the office of the undersigned after completion of your study.

KENYATTA NATIONAL HOSPITAL
OFFICE OF THE HOU DERMATOLOGY
30 JAN 2025
P.O. BOX 20723 - 00202, NAIROBI

Dr. Hannah Wanjika
HOU - DERMATOLOGY

ACN - MOPC/POPC

Vision: A world class patient-centered specialized care hospital

ISO 9001: 2015 CERTIFIED

Appendix IV: Publication Metadata

Track ID:	*4S2C4*
Main Author:	*Karen Waithera Wainaina*
Co-Author(s):	*Priscilla Angwenyi & Beatrice Wangari Ndege*
Title:	*Clinical Etiology and Histopathologic Correlation of Exfoliative Erythroderma at the Kenyatta National Hospital*
Received:	*Tuesday, 17th June 2025 at 04:20 PM*
Accepted:	*Sunday, 22nd June 2025 at 08:20 AM*
Published:	*Wednesday, 25th June 2025 at 12:41 PM*
Journal Title:	*East African Journal of Health and Science*
ISSN:	*2707-3912 (Print) and 2707-3920 (Online)*
Issue:	*Volume 8, Issue 2, 2025*
Pages:	*9-20*
CUE Points:	*Wainaina: **4**, Angwenyi: **2.67** & Ndege: **1.33***
Article DOI:	*https://doi.org/10.37284/eajhs.8.2.3210*