THE PREVALENCE AND SPECTRUM OF SKIN DISORDERS AT THE PAEDIATRIC DERMATOLOGY OUTPATIENT CLINIC OF THE CHARLOTTE MAXEKE JOHANNESBURG ACADEMIC HOSPITAL (CMJAH) IN JOHANNESBURG, SOUTH AFRICA.

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A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in partial fulfilment of the requirements for the degree of Master of Medicine in the branch of Dermatology.

Johannesburg, 2021

DECLARATION

I, Fotis Kouvelakis, declare that this research report is my own work. It is being submitted for the degree of Master of Medicine in the branch of Dermatology to the University of the Witwatersrand, Johannesburg. It has not been previously submitted for any other degree or examination at this or any other University.

This ---------- day of ----------, 2021

DEDICATION

This work is dedicated to my wife, family and friends, who have shown unwavering support and encouragement, for which I am eternally grateful.

I feel privileged to have been enriched by the wealth of knowledge and insight of the late Professor Joy Schulz, an inspiration and legend in the field of Dermatology.

I am thankful for the opportunity to have been trained by experienced and leading minds in the field of Dermatology, who have guided my path in this field in the best possible way.

ABSTRACT

Prevalence of childhood skin disease has not been extensively studied in South Africa, despite these conditions representing a significant social and economic burden. This retrospective, hospital-based study at the paediatric dermatology clinic at Charlotte Maxeke Academic Hospital in Johannesburg aimed at documenting the prevalence and spectrum of childhood skin diseases in this community. 1771 diagnostic entries showed dermatitis, skin infection, and pigment disorder categories to be most common. Atopic dermatitis was significantly prevalent (79.8%) compared to other disorders. Infections were mostly viral, predominantly represented by molluscum contagiosum, followed by dermatophytosis. This prevalence pattern resembled first-world findings, but differed to African studies whereby bacterial, parasitic and fungal infections predominated, with increasing atopic dermatitis prevalence. These findings demonstrated variation in the distribution of skin diseases between differing socio-economic environments, prompting specific interventions. High atopic dermatitis prevalence in the study population encourages further research for molecular and environmental risk factor identification, as well as optimization of management.

ACKNOWLEDGEMENTS

I wish to thank my supervisor Professor Deepak Modi for his guidance and advice in facilitating this research project, and for the invaluable teaching he has provided me with over the last six years.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

1.0 INTRODUCTION

1.1 Background

Globally, dermatological conditions contribute a significant social and economic burden. Skin diseases affect between 30% and 70% of individuals across all cultures and age groups, with significantly increased incidences in high-risk subpopulation groups (Hay, 2014).

In 2010, a study on the global burden of skin disease found that skin conditions ranged from second to the eleventh leading cause of years lived with a disability (Hay, 2014).

In South Africa, the prevalence of paediatric skin disease has not been extensively studied, the latest being done seven years ago (Katibi, 2016). These studies were done more than four decades apart, representing the pre- and post-Apartheid eras. An accurate interpretation and comparative analysis are affected due to cultural and ethnic bias represented in earlier studies.

In 2013, the Update of the Global Burden of Disease study established that skin and subcutaneous diseases were the eighteenth leading cause of global disability-adjusted life years (DALYs) and the fourth leading cause of disability worldwide (Karimkhani, 2017). The studies of paediatric age groups revealed that the predominant dermatoses were dermatitis, viral skin diseases (mainly viral warts), bacterial skin diseases (pyoderma and cellulitis) and scabies, and fungal skin infections (Karimkhani, 2017).

Studies have concluded that although dermatitis is still common in Sub-Saharan populations, there is a recurring prevalent pattern of infectious skin diseases and infestations.

The spectrum of dermatological diseases in African children are influenced by socioeconomic conditions such as overcrowded living conditions, levels of education, customs and practises of people, hygiene habits, nutritional status as well as the health-seeking behaviour of individuals (Nnoruka, 2004).

Further South African studies would clarify whether our paediatric spectrum of disease resembles that of the rest of Africa or that of developed countries. This would allow for a greater understanding of our dermatologic burden of disease.

Prevalence studies of childhood skin diseases would identify common conditions that impact the quality of life of patients and the greater community. Consequently, these could purposefully validate planning and resource-allocation for appropriate targeted interventions. Clinic-based studies provide information that can focus on practical ways of providing improved care and service.

Additionally, cumulative data obtained from multiple clinic-based, or larger community-based studies, would allow for the recognition and association between skin diseases and community-specific risk factors (Williams, 2011).

1.2 Aims

To provide the first prevalence study of skin conditions in paediatric patients at the Charlotte Maxeke Academic Hospital (CMJAH) in Johannesburg. The geographic regions of Johannesburg serviced by this institution encompass a multi-cultural, ethnically diverse and broad socio-economic spectrum of the city's population.

1.3 Objectives

1. To establish the prevalence of skin disorders at the paediatric Dermatology outpatient clinic at the Charlotte Maxeke Johannesburg Academic Hospital from 01 June 2018 to 31 May 2019.

2. To document concomitant medical co-morbidities in these patients.
3. To compare the outcomes of this prevalence study to similar studies conducted in South Africa and Sub-Saharan Africa.
4. To relate the most prevalent skin disorders at CMJAH to those representing a significant disease burden around the world.

2.0 LITERATURE REVIEW

2.1 Prevalence of childhood skin diseases

2.1.1 South African studies

There is a dearth of epidemiological research on the prevalence of childhood skin disease in South Africa. This study represents the first at CMJAH in Johannesburg. Two previous studies were conducted decades apart in different parts of the country.

Findlay et al (1974) conducted a study comprising 9877 white children in clinics in Pretoria, documenting the spectrum of skin disease.

The second study by Katibi et al in 2016 was conducted in Durban, KwaZulu-Natal (KZN). This documented the spectrum of paediatric skin disease in 419 children, skin diseases commonly seen in patients living with Human Immunodeficiency Virus (HIV), as well as comparing costs of treating different conditions.

These two studies represented data from different decades and at different political settings withing South Africa. The study conducted in 1974 was during the Apartheid era which represented divisive geographic, socio-economic and health-care circumstances in comparison to post-Apartheid way of life more than 40 years later in 2016. This was evident by the different ethnic groups represented in the studies, showing more diversity in 2016 compared to 1974. The findings of the two studies are shown in Table 2.1.

<u>Table 2.1.</u> Comparative prevalence of skin diseases of children in South Africa in 1974 and 2016

	<u>Pretoria, South Africa</u> Findlay et al, 1974	**<u>Durban, KwaZulu-Natal, South Africa</u> Katibi et al, 2016**
	DIAGNOSIS (Prevalence %) (n = 9877)	DIAGNOSIS (Prevalence %) (n = 419)
1	Atopic Dermatitis (18.7)	Atopic dermatitis (60.1)
2	Verruca vulgaris (10.7)	Viral warts (11.0)
3	Impetigo (7.8)	Seborrhoeic dermatitis (6.0)
4	Dermatitis (unspecified) (6.1)	Vitiligo (4.1)
5	Tinea capitis (5.1)	Molluscum contagiosum (3.8)
6	Seborrhoiec dermatitis (3.4)	Dermatophytosis (2.9)
7	Papular urticaria (3.2)	Acne vulgaris (1.9)
8	Pityriasis alba (3.1)	Impetigo (1.7)
9	Larva migrans (2.9)	Infantile haemangioma (1.4)
10	Scabies (2.8)	Albinism (1.2)
11	Tinea corporis 2.4%	Nappy dermatitis (1.0)
12	Plantar warts (2.3)	Papular urticaria (1.0)
13	Hand/foot eczema (2.1)	Pityriasis rosea (1.0)
14	Psoriasis (2.0)	Morphea (1.0)

In reviewing previous research done in South Africa, it was noted that atopic dermatitis was the most prevalent disease seen in both studies, showing an increase from 18.7% in 1974 to 60.1% in 2016.

Viral wart infections were second most common in both groups, making up 11% and 10.7% of diagnoses respectively.

Seborrheic dermatitis was seen in 6.0% of cases in Durban and 3.4% in Pretoria with remaining ‘unspecified’ variants representing 6.1%.

The overall pattern in these studies showed a predominance of eczematous conditions, followed by viral warts. Viral infections were higher in 2016 due to the increased amount of molluscum contagiosum cases (3.8%), which were negligible in 1974 (0.1%). The earlier study showed comparatively high impetigo values (7.8%). Scabies prevalence dropped from 2.8% in 1974 to 0.7% in 2016. The reduction of these infections over time may be indicative of improved recognition and more effective management at all levels of care.

The pigmentary disorders of vitiligo and albinism were the fourth and tenth most prevalent in Durban. These were not equally represented due to demographic variability between the study populations. This indicates the impact on outcomes between different study group variables.

2.1.2 Prevalence studies in Sub-Saharan African countries

The World Health Organization (WHO) reviewed eighteen prevalence studies for skin conditions. These were done within resource-poor African countries, altogether spanning a large geographic region. They identified tropical climate, overcrowded conditions, poor hygiene habits and limited water availability as causes for the high infection-related conditions in developing African countries. The most common skin conditions were pediculosis capitis reaching a prevalence up to 57%, pyoderma (35%), scabies (24%), tinea capitis (19.7%), viral skin diseases (9%), with dermatitis being much less common (0 - 5%) (WHO, 2005).

Table 2.2 below summarises the prevalence figures from studies done in Sub-Saharan African countries including Nigeria, Ethiopia and Tanzania. Three of the

studies were hospital-based, whereas Gibbs' study (1996) was an overview of children and adults within rural village communities.

Table 2.2. Comparative prevalence of skin diseases of children from different African studies

	Lagos, Nigeria **Ayanlowo et al** **2018**	**Southern Ethiopia** **Kelbore et al** **2019**	**North Tanzania** **Kiprono et al** **2015**	**Rural Tanzania** **Gibbs** **1996**
	DIAGNOSIS (Prevalence %) (n = 6871)	DIAGNOSIS (Prevalence %) (n = 1704)	DIAGNOSIS (Prevalence %) (n = 340)	DIAGNOSIS (Prevalence %) (n = 1114)
1	Fungal infections (16.3)	Bacterial infections (21.3)	Atopic dermatitis (31.5)	Ectoparasitic infections (49.4)
2	Atopic dermatitis (15.1)	Fungal infections (18.8)	Fungal infections (22.6)	Viral infections (9.7)
3	Infestations (13.6)	Atopic dermatitis (11.3)	Bacterial infections (13.2)	Fungal infections (9.6)
4	Viral infections (6.0)	Infestations (9.9)	Viral infections (8.8)	Bacterial infections (5.2)
5	Bacterial infections (3.8)	Contact dermatitis (5.8)	Infestations (7.4)	Tinea versicolor (3.7)
6	Acne/acneiform eruptions (3.5)	Urticaria / papular urticaria (5.8)	Papular urticaria (5.6)	Wounds (3.1)
7	Pityriasis rosea (3.4)	Viral infections (5.4)	Acne vulgaris (3.2)	Tropical ulcers (2.5)
8	Vitiligo (3.2)	Nummular eczema (4.6)	Vitiligo (2.9)	Other ulcers (2.5)
9	Childhood bullous eruption (3.2)	Vitiligo (3.6)	Pityriasis alba (2.9)	Keloids (2.1)
10	Contact dermatitis (2.5)	Pityriasis alba (3.3)	Pityriasis rosea (2.1)	Lymphoedematous keratoderma (2.1)
11	Seborrhoeic dermatitis (2.4)	Seborrheoic dermatitis (1.2)	Albinism (2.1)	Burns (1.8)
12	Lichenoid eruptions (2.4)	Acne vulgaris (1.1)	Nevi (2.1)	Lymphoedema (1.5)

An overall large proportion of infection-related skin diseases predominated in the African studies. Despite this finding, atopic dermatitis was still relatively common in these countries. The exception to this was noted in the rural study, whereby a significant proportion of cases represented transmissible causes, and atopic dermatitis did not feature in the most prevalent group, but rather occurred rarely (Gibbs, 1996). This finding highlighted the impact of risk factors such as rural living conditions on skin disease, and further the fact that different locations have different health care needs.

2.1.3 First-world clinic-based perspectives on childhood skin disease

Hospital-based studies from a Chinese paediatric dermatology clinic, and a Swiss paediatric clinic are tabulated (Table 2.3) to compare paediatric skin disease patterns in a first-world setting to developing countries, and particularly South Africa.

Table 2.3. Prevalence of skin diseases of children as documented in studies from China and Switzerland

	Hong Kong, China **Hon et al, 2004**	**Aargau, Switzerland** **Wenk et al, 2003**
	DIAGNOSIS (Prevalence %) (n = 331)	DIAGNOSIS (Prevalence %) (n = 1105)
1	Endogenous eczema (33.4)	Atopic dermatitis (25.9)
2	Melanocytic nevi (10.2)	Pigmented nevi (9.2)
3	Viral warts (5.7)	Viral warts (5.0)
4	Vitiligo (5.39)	Molluscum contagiosum (4.85)
5	Epidermal and sebaceous nevi (5.12)	Eczema NOS (non-atopic) (3.95)
6	Vascular nevi (4.31)	Haemangioma (2.9)
7	Pityriasis alba (3.23)	Impetigo contagiosa (2.9)
8	Other dermatitis (2.96)	Acne vulgaris (2.8)
9	Tinea infections (2.70)	Urticaria (2.8)
10	Urticaria (2.70)	Pityriasis alba (2.6)
11	Acne vulgaris (2.43)	Alopecia areata (2.2)
12	Neurofibromatosis (1.62)	Fungal infections (2.1)
13	Molluscum contagiosum (1.62)	Psoriasis (2.0)
14	Impetigo/folliculitis/cellulitis (1.35)	Parasitic infections (1.8)

First-world clinic-based findings (Table 2.3) showed atopic dermatitis to be remarkably more common than other conditions, as was seen in the South African studies. Viral warts showed a similar proportion to South African studies, in that they were in the top three overall diagnoses, and were the most common of all infections. Bacterial and fungal infections were proportionately lower than those seen in African studies, with more abundant presentations of pigmented nevi. The Swiss study showed haemangiomas and acne vulgaris to be more commonly seen than bacterial and fungal infections. Although these are individual clinic-based examples and may not represent the broader community in its entirety, this data is suggestive of differing patterns of skin disease in first world settings, possibly due to geographic environmental conditions, genetic variations, and resource-dependent factors such as health-care infrastructure.

It has been found that despite the predominance of skin infections within poverty-stricken and tropical countries, the global high burden of eczema-related disability has been consistent, with prevalence increasing in parts of the world (Hay, 2014).

The information reviewed above corroborated this description as it showed a steep rise of atopic eczema prevalence in South Africa over the last four decades. Additionally, this condition predominated in developed countries and to a lesser extent, was also prevalent in Africa. In view of these findings, a review of atopic dermatitis was pertinent in the scope of analysing paediatric skin disease.

2.2 Atopic dermatitis representing a prevalent skin condition globally

Larger worldwide prevalence studies on childhood skin diseases prominently focus on atopic dermatitis. This was the subject of multiple publications that ranged from smaller centre-based to larger national population-based studies. Systematic reviews that incorporated data from worldwide studies such as the International Study of Asthma and Allergies in Childhood (ISAAC) study which represented a standardised manner to assess the rate of prevalence of this condition globally over time.

2.2.1 Atopic dermatitis largely studied throughout the world

Nationwide prevalence data that assessed demographic associations to atopic eczema was published in the United Kingdom (UK) (De Lusignan, 2020) and United States (USA) (Shaw, 2011).

A study by De Lusignan et al in the UK (2020), utilised a different approach to centre-based study models seen in Africa. They incorporated a larger population group that consisted of patients attending general practitioners throughout England (De Lusignan, 2020). They utilised pre-existing databases of the Royal College of General Practitioners Research and Surveillance Centre (RCGP RSC) to obtain data pertaining to a diagnosis of eczema. The database was linked to 293 general practitioner practices, which contained 3.85 million patient records (De Lusignan, 2020). Prevalence of atopic eczema was related to patient age, socio-economic status, ethnicity and rural/urban residence (De Lusignan, 2020). In this large sample of 54 659 patients with eczema throughout the country, an equal distribution of 9.6% prevalence was seen in both sexes. Of significance, eczema was more common in black and Asian ethnic groups (16.5% in each group) with white patients being least affected (8.4%). Eczema was more common in urban dwellers with a higher socio-economic status (De Lusignan, 2020).

2.2.2 Systematic reviews of atopic dermatitis

Worldwide atopic dermatitis prevalence studies were conducted by researchers from multiple centres. A well-known and commonly referenced study within the scope of global atopic eczema prevalence statistics was the ISAAC study. This represented the largest global, population-based data collection, and demonstrated an effective study design that ensured better diagnostic accuracy and standardization of information obtained from all continents (ISAAC, 1998).

Deckers et al (2012) investigated incidence and prevalence of atopic eczema from 1990 to 2010. Seven databases had resulted in 69 publications being assessed out of 2464 citations. This study showed an increasing prevalence of atopic dermatitis in Africa, with lifetime prevalence in South Africa having risen from 15.5% to 26.2% over a seven-year period (Deckers, 2012).

It was concluded that prevalence trends for atopic dermatitis were not consistent globally, and this was also found in the systematic review by Bylund et al in 2020. Their study reviewed data from 378 publications from 1958 to 2018. This showed atopic dermatitis to be more prevalent in the 21st century compared to the 20th century (Bylund, 2020) with a point prevalence of atopic dermatitis symptoms in children ranging broadly between 1.7% - 32.8% (Bylund, 2020).

Both of these expansive studies found drawbacks in their data collection processes, as the distribution of available studies was uneven throughout the world. Heterogeneity between the study designs and variables, and more significantly a lacking gold standard for universally defining atopic dermatitis (Deckers, 2012), made overall interpretation of atopic eczema prevalence and trends difficult (Bylund, 2020).

The ISAAC study addressed these drawbacks and presented a design model to improve the consistency and reliability of studies by conducting a standardised method of data collection (Bylund, 2020). This was done through the use of a simply designed questionnaire that focused on identifying definitive symptoms of atopic dermatitis within specific age groups (13 -14 years). The research spanned nearly 60 countries with 463,801 participants in Phase One (ISAAC, 1998). This model was replicated after 5-10 years in Phase Three, with 302,159 participants (13 – 14 years), in addition to 187,943 (6 – 7 years). This study developed a standardised approach for the collection and comparison of data at different time periods. This showed a more reliable method of assessing the rate of change of prevalence of atopic eczema, asthma and allergic rhino-conjunctivitis (Williams, 2008). The design of progressively refined diagnostic tools for atopic eczema has been ongoing with different criteria aimed at hospital or community settings used in the 1990’s at which time the United Kingdom Working Party diagnostic criteria was validated internationally, followed by the ISAAC criteria (Lee, 2016). Advances in this regard may see potential improvement in statistical strength, by proposing the use of a novel REACH (Reliable Estimation of Atopic Dermatitis in Childhood) questionnaire. Active model-design initiatives occurring over decades highlights the key role of accurate diagnosis of atopic dermatitis for worldwide analysis (Lee, 2016).

ISAAC results showed global variability of atopic dermatitis prevalence ranging from less than 2% to 20% in different regions, and deduced that atopic eczema reached a plateau within any given population group (Williams, 2008). Furthermore, data comparisons after 5-10 years facilitated annual rate calculation, further guiding research and resources in those areas most requiring interventions (Williams, 2008). A rising prevalence in developing African countries such as Kenya and Algeria, as well as multiple countries in Southeast Asia, Mexico and Chile was found (Williams, 2008).

2.3 Atopic dermatitis impacting quality of life

The focus of atopic eczema within a vast array of existing skin diseases, although partly due to the widespread prevalence, significantly imposes a large burden to the quality of life of patients, their families, as well as conveying a significant cost burden (Mar, 1999).

2.3.1 Impact of atopic dermatitis on the patient

Atopic dermatitis has considerable medical, psychological, social and financial consequences for patients and their families or caregivers (Carroll, 2005). These effects lead to a lower quality-of-life score in these patients due to reduced social, emotional and mental functionality, as tested in different studies by Kiebert et al and Linnet et al (Carroll, 2005).

Psychosocial problems encompass anxiety, frustration, embarrassment, and anger owing to the effect of this disease on physical appearance (Carroll, 2005). These factors lead to behavioural dysfunction, such as increased dependency on others, overprotectiveness by others, and impedance of physical activities (Carroll, 2005)

Sleep disturbance is a well-documented significant morbidity resulting from pruritis, the itch-scratch cycle, and is worsened by the underlying anxiety seen in some patients. Pruritis affects patient's ability to fall asleep and wakes them from sleep, as seen in 84% and 79% respectively in a study by Yosipovitch et al (Carroll, 2005). According to Reid et al, children with atopic dermatitis experience an average of two

hours of sleep loss, which has implications of daytime drowsiness and reduced school performance (Carroll, 2005).

2.3.2 Impact of atopic dermatitis on the family

Manuel et al provided a thorough insight into the impact of atopic dermatitis on the family. Their study examined nine categories of family impact which included: sleep difficulties, lifestyle modification, treatment challenges, time management, social impact, school and day-care issues, family activities, financial stress and personal strain (Carroll, 2005).

Of note, parents caring for children with atopic dermatitis use two to three hours per day on child-care and lose one to two hours of sleep per night tending to symptoms (Carroll, 2005). The long-standing preoccupation with eczema-related issues results in strained interpersonal relationships among spouses and siblings who may not receive the same level of attention (Carroll, 2005). In addition, the financial impact can be considerable because of time out of work, the cost of treatments and dietary alterations (Carroll, 2005). These multiple cumulative factors lead to a lower quality of life for families with children who have atopic dermatitis than those with healthy children (Carroll, 2005).

Ideally, clinicians should enquire about all repercussions of atopic dermatitis in order to gain a comprehensive understanding of the overall impact, severity and detriment to the patient's quality of life. This would prompt a more holistic approach to treatment.

Holistic approach to management proved to be successful in the Berlin Education Programme (Wenninger, 2000) which primarily focussed on providing adequate education about atopic dermatitis to caregivers. This Programme consisted of six sessions of two-hour duration group sessions whereby parents of children with atopic dermatitis interacted with physicians, psychologists and nutritionists (Wenninger, 2000). There was a resultant improvement of quality of life of these family members owing to provision of information and better psychosocial support which translated into more efficient use of treatment, cost reductions and better

coping of these parents (Wenninger, 2000). This concept represents a cost-effective intervention within the specialist clinical setting of the current study population.

2.4 The cost of skin diseases

Multiple studies have been done to analyse cost factors, and highlight the significant economic burden that atopic dermatitis has in South Africa and throughout the world.

In South Africa, Katibi et al conducted a cost profile per patient to compare the expense of common paediatric skin conditions, including atopic dermatitis, viral warts, seborrheic dermatitis, vitiligo, molluscum contagiosum, dermatophytosis and acne vulgaris (Katibi, 2016). Although the exact values will change over time, it is the relative difference of expense between these conditions in addition to their comparative frequency within the population which is important. Diseases incurring the highest costs should warrant implementation of intervention models, to actively reduce the financial burden as far as possible. According to South African (Katibi) and worldwide statistics (Mar, 1999), atopic eczema features prominently which makes this condition expensive to treat.

Studies assessing direct costs of atopic eczema (emergency room consultations, physician visits and prescription medication) have shown this condition to be a significant financial burden internationally (Carroll, 2005). A systematic review by Ellis et al found the cost of atopic eczema with associated co-morbidities in the USA to be $900-million in 2002, which increased substantially from $364-million in 1990 (Ellis, 2002). Heavy costs were also recognised in other developed countries such as the United Kingdom where it cost $721-million to treat this condition in 1996 (Ellis, 2002). Atopic eczema cost $250-million more to treat than psoriasis ($649.6-million) in 2002 (Javitz, 2002). Apart from these direct treatment figures, expenses pertaining to non-prescription medication, over-the-counter purchases, allergy testing and time lost at work due represents indirect costs, which may be contribute as much as three-quarters of overall costs (Carroll, 2005).

3.0 METHODS

3.1 Study Design and Site

This was a cross-sectional, retrospective, hospital-based study conducted at the paediatric dermatology specialist clinic at CMJAH.

3.2 Study Population

Data for this study was obtained from patient files of all children who attended the paediatric dermatology clinic. These included information about new patients as well as patients previously seen. The age range of patients that attended this clinic was from neonatal to 18 years of age, and was representative of multiple ethnicities.

3.3 Sample Size

A total number of 1675 patient files were assessed. Repeat visits of patients to the clinic in the studied time period or any duplicate files for the same patient were not included.

3.4 Material

A data-collection sheet was created to record the necessary patient information from clinic files which included categories for: age, gender, primary skin diagnosis, second skin diagnosis and co-morbidities (APPENDIX A). Patient diagnoses were based on the clinical observation and assessment of the treating doctor or guided by histology results.

3.5 Data Analysis

The files of 1675 patients who attended the clinic from 01 June 2018 to 31 May 2019 were reviewed for data collection. Relevant data in keeping with parameters

indicated on the collection sheet was incorporated into a Microsoft Excel™ spreadsheet.

A descriptive analysis of data was carried out as follows: categorical variables were summarised by frequency and percentage tabulation and illustrated by means of bar charts; and continuous variable (age) was summarised by the mean and standard deviation. The collected data was interpreted by sorting of individual parameters to allow for necessary comparisons. The grouping and ranking order of all individual diagnoses documented was done using Microsoft Excel. Male and female data was plotted individually for comparative purposes. Data was used to categorise patients into age groups that included: infancy (0-<2years), pre-school ages (2-5years), school ages (6-11years), and adolescent age (12-18years). Sorting of the data according to different variables allowed for interpretation of skin disease prevalence from these perspectives.

3.6 Ethics

Ethical clearance was granted by the University of the Witwatersrand Human Research Ethics Committee (Medical) prior to the commencement of data collection (APPENDIX B).

Permission from the Chief Executive Officer of CMJAH was granted to enable access to patient files for this study.

3.7 Funding

Private funding was used by the principal researcher for transport, printing and photocopying costs that were incurred.

4.0 RESULTS

4.1 Characteristics of study participants

Data for a total of 1675 of patients aged between 0 and 18 years was analysed. This was done at the paediatric dermatology specialist clinic at CMJAH, and included all patients seen from 01 June 2018 to 31 May 2019. Repeat visits by the same patients were not included.

4.2 Sex and age characteristics of the population

The study consisted of 850 (51.0%) males, and 825 (49.0%) females. The male to female ratio was 1.03. Ages ranged from neonatal to 18 years, with a mean age of 6.9 years (standard deviation of 4.51). The study group was classified into age groups that included infants (0 - <2 years old), pre-school age (2 – 5 years old), school-aged (6 – 11years old), and adolescents (12 – 18years old). Most visits were by school-aged children (38.27%), followed by the pre-school group (29.37%), adolescents (18.75%), with fewest patients being infants (13.61%).

4.3 Spectrum of skin disorders

A total of 1771 diagnosis entries were documented amongst the 1675 children. This indicated that 96 (5.73%) patients had more than one skin condition.

Fifty-one skin conditions were recorded and listed into thirteen dermatological categories. These are shown in Table 4.1.

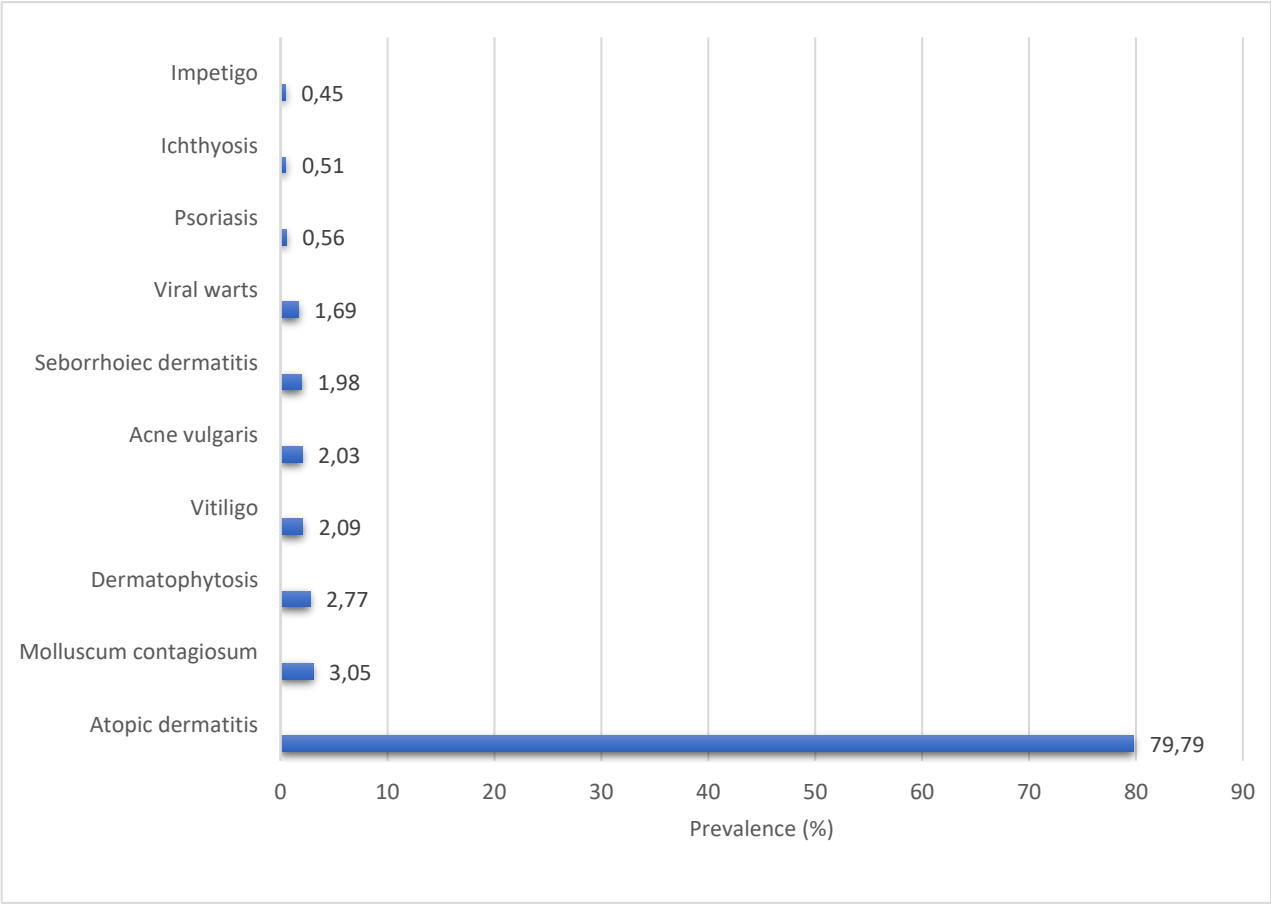
Table 4.1. Prevalence of skin conditions and gender distribution within the study group

Cutaneous Lesion	Male	Female	n (%)
Dermatitis			**1453 (82,04)**
AD	727	686	1413 (79,79)
Seborrhoeic dermatitis	14	21	35 (1,98)
Erythroderma	2	1	3 (0,17)
Nappy dermatitis	1	0	1 (0,06)
Contact eczema	1	0	1 (0,06)
Infections			**156 (8,81)**
Viral			89 (5,03)
Molluscum contagiosum	29	25	54 (3,05)
Viral warts	13	17	30 (1,69)
Herpes simplex virus	2	3	5 (0,28)
Fungal			50 (2,82)
Dermatophytosis	31	18	49 (2,77)
Pityriasis versicolor	0	1	1 (0,06)
Bacterial			9 (0,51)
Impetigo	2	6	8 (0,45)
Folliculitis	1	0	1 (0,06)
Parasitic			8 (0,45)
Scabies	4	4	8 (0,45)
Pigmentary			**52 (2,94)**
Vitiligo	12	25	37 (2,09)
Albinism	6	5	11 (0,62)
Post-inflammatory pigmentation	2	1	3 (0,17)
Nevus depigmentosis	0	1	1 (0,06)
Appendages			**43 (2,43)**
Acne vulgaris	15	21	36 (2,03)
Nail dystrophy	2	2	4 (0,23)
Alopecia areata	1	1	2 (0,11)
Miliaria crystallina	1	0	1 (0,06)
Papulosquamous			**20 (1,12)**
Psoriasis	4	6	10 (0,56)
Pityriasis alba	2	2	4 (0,23)
Pityriasis rosea	2	1	3 (0,17)
Pityriasis lichenoides chronica	0	1	1 (0,06)
Lichen nitidus	0	1	1 (0,06)
Lichen striatus	0	1	1 (0,06)
Genodermatoses			**18 (1,02)**
Ichthyosis	2	7	9 (0,51)
Congenital melanocytic naevus	3	0	3 (0,17)
Epidermal naevus	2	0	2 (0,11)

Epidermolysis bullosa	1	0	1 (0,06)
Neurofibromatosis	1	0	1 (0,06)
Xeroderma pigmentosum	1	0	1 (0,06)
Darier's disease	0	1	1 (0,06)
Vascular			**8 (0,45)**
Infantile haemangioma	0	4	4 (0,23)
Leukocytoclastic vasculitis	1	2	3 (0,17)
Kaposi sarcoma	1	0	1 (0,06)
Dermis & subcutaneous nodules			**4 (0,23)**
Mastocytosis	1	1	2 (0,11)
Panniculitis	1	1	2 (0,11)
Drug reaction			**3 (0,17)**
Stevens Johnson Syndrome	0	2	2 (0,11)
Lichenoid drug eruption	1	0	1 (0,06)
Urticaria			**3 (0,17)**
Chronic urticaria	3	0	3 (0,17)
Vesicobullous			**1 (0,06)**
CBDC	1	0	1 (0,06)
Connective tissue diagnosis			**1 (0,06)**
Systemic lupus erythematosus	0	1	1 (0,06)
Miscellaneous			**9 (0,51)**
Acanthosis nigricans	1	1	2 (0,11)
Keratosis pilaris	1	1	2 (0,11)
Acrodermatitis enteropathica	1	0	1 (0,06)
Arthopod bite	1	0	1 (0,06)
Calcinosis	1	0	1 (0,06)
Granuloma anulare	1	0	1 (0,06)
Hypereosinophilic syndrome	1	0	1 (0,06)

The most prevalent skin disorders according to categories were dermatitis (82.04%), infections (8.81%), pigmentary conditions (2.94%), appendageal disorders (2.43%), papulo-squamous conditions (1.12%) and genodermatoses (1.02%) (Table 4.1). The remaining categories each represented less than 1.0% prevalence in the study population.

The most common individual diagnoses are shown in Figure 4.1 below. These were atopic dermatitis (79.79%), molluscum contagiosum (3.05%), dermatophyte infections (2.77%), vitiligo (2.09%) and acne vulgaris (2.03%), seborrheic dermatitis (1.98%), viral warts (1.69%). Thereafter, individual disorders represented less than 1.0% overall prevalence.



<u>Figure 4.1</u>. Most prevalent skin disorders seen among the study population

Dermatophyte infections (Table 4.2) in descending relative proportion, included tinea capitis (69.0%), tinea corporis (18.4%), tinea facialis (6.12%), and tinea pedis (6.12%).

Table 4.2. Dermatophyte infections seen in the study population

DERMATOPHYTE INFECTIONS	MALES (%)	FEMALES (%)	PROPORTION TO OVERALL DERMATOPHYTE INFECTIONS (%)
Tinea capitis	64.7	35.3	**69.0**
Tinea corporis	55.6	44.4	**18.4**
Tinea facialis	66.6	33.3	**6.12**
Tinea pedis	66.6	33.3	**6.12**

4.4 Frequency and patterns of diagnoses in relation to sex and age

An almost equal proportion of atopic dermatitis was seen in males (51.45%) and females (48.55%). Similar prevalence in males (53.70%) and females (46.30%). was also seen for molluscum contagiosum. More males presented with dermatophyte infections (63.27%), and particularly showed higher proportion of tinea capitis infections within this group (69.00%) (Table 4.3). Conditions more commonly seen females included vitiligo (67.57%), acne vulgaris (58.33%) and seborrheic dermatitis (60.00%).

Table 4.3. Distribution of most common skin diseases by age group

	0 - < 2 years (n = 228)	2 – 5 years (n = 492)	6 – 11 years (n = 641)	12 – 18 years (n = 314)
1	Atopic dermatitis 83.8%	Atopic dermatitis 85.0%	Atopic dermatitis 85.5%	Atopic dermatitis 81.5%
2	Seborrhoeic dermatitis 6.6%	Molluscum contagiosum 5.7%	Dermatophyte infections 4.1%	Acne vulgaris 9.2%
3	Molluscum contagiosum 2.6%	Dermatophyte infections 3.7%	Molluscum contagiosum 3.1%	Viral warts 2.5%
4	Viral warts 1.8%	Vitiligo 2.6%	Vitiligo 2.7%	Vitiligo 2.2%
5	Infantile haemangioma 1.3%	Seborrhoeic dermatitis 2.0%	Viral warts 1.7%	Dermatophyte infections 1.3%
6	Scabies 1.3%	Viral warts 1.4%	Seborrhoeic dermatitis 1.1%	Psoriasis 1.1%

Table 4.3 shows the most common conditions seen per age group. Regarding the most common conditions seen, atopic dermatitis was significantly more common than all other conditions. It was predominant within all age-groups (exceeding 81% in all groups). Infections of the skin varied within the different age groups. Viral warts were consistently seen in all groups whereas dermatophyte infections were uncommon in infants, peaked in the pre-school and school-aged groups, with few cases in adolescent patients. Molluscum contagiosum was commonly seen in the infant, pre-school and school-aged children, but not in the adolescent group which showed the most cases of acne vulgaris. Scabies infection was uncommon (0.45%), with equal proportion of cases seen in infants and pre-school children.

4.5 Medical co-morbidities in the study population

A very small quantity of medical co-morbidities was identified in the patient files seen. Only 1 % of the total study group had a clearly documented co-morbidity. Of this group, 26.67% consisted allergy-mediated illnesses of allergic rhinitis, asthma, and allergic conjunctivitis. The skin pathology in all of these patients was atopic dermatitis. HIV infection comprised 20% of overall co-morbidities documented. This condition was seen in patients that presented with atopic dermatitis, seborrheic dermatitis and previous herpes zoster infection. Congenital adrenal hyperplasia (CAH) was reported in two patients with acne vulgaris. The remaining co-morbidities were unrelated to the skin pathology diagnosed. Data on medical co-morbidities was insufficient, and did not significantly represent the study population.

5.0 DISCUSSION

5.1 Atopic Dermatitis

5.1.1 Variation in the prevalence of atopic dermatitis

5.1.1.1 Atopic dermatitis in South Africa and relation to sex and age

Atopic dermatitis was the most prevalent skin condition in all of the South African studies. This signifies this condition to be a chronic burden in South Africa, affecting diverse communities for at least 45 years. The proportion of cases increased from 18.7% in 1974, to 60.1% in 2016, and currently recorded at 79.8% in clinic-based environments. Along with a significant rise of prevalence recorded, atopic dermatitis was currently found to be most prevalent in all age groups (Table 6). The number of cases increased from 191 in infants, to 418 in pre-school ages, followed by the highest number of 547 in school-aged children. Despite a decline to 255 in adolescents, a proportional tapering off of this prevalence was not seen at CMJAH.

The relative prevalence of 83.8%, 85.0%, 85.5% and 81.5% shown in the respective age-groups at CMJAH as compared to a decline seen in Durban from 59.3% in school-aged children to 12.1% in adolescents (Katibi, 2016).

5.1.2 Factors causing variation in prevalence of atopic dermatitis

5.1.2.1 Clinic–based factors

Referral structures

Prevalence studies that are institution-based may also be variably influenced by referral-related protocols. Differences in the proportion of skin conditions within this study could partly be attributed to the referral patterns in this community. The study was conducted at a tertiary hospital that accepts patients upon being referred from less-specialised institutions that seek further specialist assistance.

The South African Essential Drugs List (EDL) for Paediatrics (DOH, 2008) offers guidelines for treatment of skin conditions available at Primary Health Care level. These protocols in conjunction with skill and medication-based resources available in smaller centres, may dictate the types of skin conditions referred to the specialist centre. Acute, uncomplicated skin conditions that are affordable to treat would more likely be managed at this level, whereas chronic, unresolving conditions that may recur or complicate would preferentially be referred.

As indicated in the EDL, the treatment available for atopic eczema, consists of emollients, 1% hydrocortisone cream or doctor-initiated 0.1% betamethasone ointment, and antihistamines (DOH, 2008). These options, when available, represent a limited range in managing atopic eczema. Such patients warrant referral and are seen at tertiary centres more than infections that are likely treated successfully with a single prescription of fewer medications that are commonly available (DOH, 2008).

Patient review and discharge protocols

From the data collected, it was noted that many patients with atopic dermatitis were controlled, showing no active skin changes, often on a consecutive follow-up basis. This indicated a tendency to retain patients with atopic dermatitis at the specialist clinic. A low discharge rate of this subset of patients relative to continuous flow of new patient presentations would favour a relatively high proportion of these cases. This would be seen within all age-groups, in view of the same patients remaining within the clinic system for the duration of years.

The onset of second skin conditions in patients already known to have atopic dermatitis would also influence prevalence proportion. 73% of adolescent patients with acne vulgaris also had atopic dermatitis. By these patients remaining within the same treating clinic resulted in the continuous documentation of atopic eczema, regardless if this had been resolved, with a different skin condition needing active management. The infrequency of downgrading patients to smaller facilities would require adequate staff and medical resources in these peripheral areas to allow for an adequate distribution of patient care where specialist treatment is no longer required.

5.1.2.2 Ethnic variation in the study populations

The study conducted in 1974 consisted of white children, during the Apartheid era in South Africa. This study therefore did not cover a realistic portrayal of the community at large, but rather an ethnically biased view of skin disease. This would consequently have limited the identification of linked risk factors in the population, such as socio-economic and lifestyle impact on prevalent disorders.

In contrast to 1974, the study done in 2016 comprised of one white child (0.2%), with 87.6% black, 9.5% Indian and 2.6% mixed-race children (Katibi, 2016). Although this represented a wider ethnic spectrum, the distribution was grossly uneven. This highlighted a limitation of centre-based prevalence studies, as patients who presented to a public hospital specialist clinic did not portray an accurate societal ratio as that of the community at large. The notable discrepancy of 18.7% prevalence of atopic dermatitis in white children and 60.1% in a study group of over 99% non-white children, underscored inherent predispositions for this condition between ethnic groups.

Studies in genetic research showed associations between atopic dermatitis and genetic loci unique to ethnic groups (Kaufman, 2018). Molecular mechanisms may therefore determine a pattern of eczema distribution within South African communities. Larger population studies examining prevalence of atopic dermatitis in each ethnic group would be valuable to establish local genetic influences.

A nationwide study done in the United Kingdom recently found the prevalence of atopic dermatitis to be higher in Black (16,5%) and Asian (16,4%) population groups across the country, as compared to the White group (8,4%) (De Lusignan, 2020). Similarly, the association of higher prevalence in black and multi-race ethnic groups was also demonstrated in an eczema prevalence study in the United States (Shaw, 2011).

Another association between ethnicity and atopic dermatitis was demonstrated by Kaufman et al. whereby the rate of eczema was higher in African countries than in India and parts of Europe (Kaufman, 2018) and higher prevalence representation thereof in African-American children compared to European-American children within the United States (Kaufman, 2018). In the United Kingdom it was similarly noted that

white children with atopic dermatitis represented roughly half (8,7%) the proportion of cases compared to Black-Caribbean children (16,3%) that were born in London (Kaufman, 2018).

A collaboration of Asian, Hispanic and African data has allowed for the revelation of 31 loci relating to atopic dermatitis risk. These loci contain 15 million genetic variants within these ethnic groups, with ongoing research done by the genome-wide association (GWAS) (Kaufman, 2018). The mutations implicated in this condition affect the function of the skin's epithelial barrier as well as immune regulation. The well-documented Filaggrin (FLG) loss-of-function mutations has been shown to be less commonly associated with atopic dermatitis in people with African ancestry, with no association seen in Ethiopian studies (Kaufman, 2018). A mutation encoding for a different filaggrin-related protein, known as FLG-2, was however found to be more commonly associated to atopic dermatitis in Ethiopians and Americans with African descent, yet unrelated in European groups (Kaufman, 2018). Additionally, immune-related genes have also been specifically linked to different ethnic groups for example STAT6 and thymic stromal lymphoprotein (TSLP), Interleuken-7 receptor (IL-7R), Toll-like receptor 2 (TLR2), as well as antimicrobial peptide mutations (b-defensin B1) (Kaufman, 2018). These findings hold significant relevance as immunological targets can be used for the future development of specific treatment for atopic dermatitis within the relevant ethnic population groups. This could prove to be more clinically effective and reduce overall costs as compared to the use of a more broad, generalised treatment approach in all parts of the world.

5.1.2.3 Environmental and socio-economic factors

Climate differences such as higher humidity and lower latitude of Kwa-Zulu Natal could partially explain the lower prevalence rate Durban compared to current findings in Johannesburg (Kaufman, 2018).

Large national-based prevalence studies in the United Kingdom (De Lusignan, 2020) and United States (Shaw, 2011) showed higher prevalence of atopic dermatitis in children living in metropolitan areas. This factor would also pertain to an ongoing migration of people from rural to urban areas in pursuit of employment opportunities

in South Africa. Quantifying this phenomenon was not explored in this study, however highlighted the relevance of population dynamics between rural versus urban populations that may be differentially represented at specialist clinics in different provinces. This could locally influence specific disease prevalence. If the specialist clinic in Durban comprised a larger proportion of rural patients, it may have resulted in a relatively lower atopic dermatitis prevalence, in comparison to CMJAH seeing more urban-based patients.

Studies worldwide have cited socio-economic and environmental factors as contributing triggers that can be implicated in the distribution of specific disease to certain locations (Mar, 1999).

Environmental factors that influenced skin disease distribution in Nigeria included overcrowding and areas with poorer infrastructures (Nnoruka, 2004). Broadly, patterns of skin diseases could be affiliated to lifestyle determinants of people in a community, encompassing their level of education, strength of cultural beliefs, traditional customs, hygiene habits, nutritional status, as well as political factors (Nnoruka, 2004).

The increasing prevalence of atopic dermatitis in African countries such as Nigeria and Ethiopia (Ogunbiyi, 2004) corresponded to increased industrialization in those countries and it may be a consideration that the increased documentation of atopic dermatitis has resulted from better health-care access in urban settings (Ogunbiyi, 2004). Urbanisation has represented higher workplace and home-based chemical exposure, dietary changes and use of alternative herbal substances. Such associations may describe triggers to this condition. (Ogunbiyi, 2004). Common use of traditional topical products was particularly seen in the region of Tigray, Ethiopia whereby the consequence of applying cultural mixtures of herbs, soil, coffee, and oils resulted in a high prevalence of contact dermatitis in this community. The reliability of deciphering between different types of eczema is important in identifying local habits that can be addressed directly and modified. Locally sourced cosmetic and skin-lightening creams further increased such cases (Marrone, 2012). Such topical products are also familiar in the South African setting, and may result in misdiagnosis if not asked about or considered within the paediatric setting.

Even though skin infections in children decrease with the improvement of socio-economic circumstances and better hygiene practices over time (Ogunbiyi, 2004), it has subsequently been considered that more regular bathing, hand-washing and wiping of the skin has contributed to the incline of atopic dermatitis (Shaw, 2011) in developing countries such as Nigeria, where this condition is increasing (Ogunbiyi, 2004).

Rural dwellings constructed from mud and clay potentially convey a lower risk for atopic dermatitis in comparison to homes made of brick and wood materials (Marrone, 2012). In the United Kingdom De Lusignan et al considered more associations including a higher exposure of ultraviolet radiation, cooler air temperatures and increased central heating use (De Lusignan, 2020). Heavy pollution has also been linked to increased dermatitis in urban areas (De Lusignan, 2020). Higher exposures to synthetic fabrics in urban environments, such as those found in home insulation, carpets and bed linen have been associated to atopic dermatitis, thereby relating the rise of its prevalence to progressing urbanization and improved socio-economic living conditions (Carroll, 2005).

A scenario that could summarise the above-mentioned multifactorial elements was speculated by Williams et al (2008). The increasing rate of atopic dermatitis may be due to an interplay between genetic predisposition, an inflamed skin state, and allergen exposure from a young age. This state of skin inflammation, which is more vulnerable to allergens, may be due to more frequent exposure to harsh cleansing soap products from birth. Within the context of urbanisation, the rise of cases in population groups over time would be expected (Williams, 2008).

5.2 Skin Infections

5.2.1 Infections in South Africa

Infections of the skin represented the second most prevalent condition categorically. The overall prevalence of 8.81% was lower than that seen in the other South African studies, which were 16.7% in 2016 (Katibi, 2016) and overall exceeded 30% in 1974 (Findlay, 1974). This reduced proportion of skin infections over time would represent

better recognition and treatment of these conditions at a non-specialist level of care. Environmental and socio-economic conditions within different cities, and differences in the proportion of rural areas covered by specialist clinics would contribute to differing overall outcomes. Viral infections represented the majority of infections in this study (5.03%). Molluscum contagiosum comprised 60.7% of these, and was the most commonly diagnosed individual skin infection, followed by viral warts (1.69%).

5.2.1.1 Molluscum contagiosum

A systematic review of molluscum contagiosum found the worldwide overall prevalence of this condition to be between 5.1% - 11.5% from birth to 16 years of age (Olsen, 2014). It was found that most infections typically occurred between 1 and 4 years old with genders equally affected (Olsen, 2014). This corroborated with my findings that showed 60.7% of cases occurring in the first 5 years of life, affecting males and females almost equally (54% males, 46% females).

The overall prevalence of 3.05% showed a three-fold increase since 1974 (1.1%). This increased rate and high prevalence of these infections within South Africa may be due to dynamic risk factors, and could mirror the corresponding rise of atopic dermatitis also seen within this study population. This association has been seen in isolated studies (Olsen, 2014). A warm climate, frequent use of swimming pools, and sharing of towels and sponges are risk factors (Olsen, 2014) of molluscum contagiosum. These factors would be relevant within a setting of increasing urbanisation whereby children interact closely in playschool environments and may be introduced to swimming activities at school.

5.2.1.2 Viral warts

Viral warts represented the second most prevalent infections in the study group (1.7%). These were the most common of the documented infections in previous South African studies, with significantly higher prevalence of 11% in Durban (Katibi, 2016) and 10.7% in Pretoria (Findlay, 1974). African studies showed viral warts to fall within the top five commonest diagnoses with similar prevalence rates of cases in

tertiary centre studies (6.0% in Nigeria, 4.4% in Tanzania) (Ayanlowo, 2018) (Kiprono, 2015) as well as in a rural setting (6.4% in Tanzania) (Gibbs, 1996).

Similar findings were seen in China and Switzerland with 5.66% (Hon, 2004) and 5.0% (Wenk, 2003) prevalence respectively.

These comparisons indicated a consistent presence of viral warts in different population groups over time, and may indicate a lesser influence of socio-economic and environmental risk factors.

A study by Van Haalen et al in 2009 found the overall presence of viral warts to be between 3 to 20%, affecting males and females equally (Van Haalen, 2009). This corresponded to the current findings as 57% of cases were in females and 43% in males. The study also concluded that infection rate was associated with exposure to a high viral concentration such as in homes or classrooms in the presence of multiple people already infected (Van Haalen, 2009). The immune system adaptation to multiple viral subtype exposures may also influence risk of infection in individuals differently, whereas direct environmental conditions such as barefoot sport activities and use of public swimming pools and showers were not proven to be significant in viral spread (Van Haalen, 2009).

Ayanlowo et al highlighted the possibility of generalized warts as a possible indicator of underlying immunosuppression (Ayanlowo, 2018), in view of the high 11% prevalence in KwaZulu Natal, whereby over half of these patients were HIV-positive (Katibi, 2016). Further studies examining the prevalence of skin conditions in HIV positive children would be useful to further validate this association.

5.2.1.3 Dermatophyte infections

Fungal skin infections were the third most common diagnosis in the study group with a prevalence of 2.82%. Dermatophytosis most commonly comprised of tinea capitis (69.0%), followed by tinea corporis (18.4%), tinea facialis (6.1%) and tinea pedis (6.1%). The majority of fungal infections occurred in males (63.3%). These infections featured in the pre-school aged children (3.7% in 2–5 years old), peaked at school-going ages (4.1% in 6–11 years old), with a marked decrease in adolescents (1.3%

in 12–18 year-olds). Table 3 summarises the distribution of fungal infections in the study group.

Tinea capitis affected males nearly twice as much (64.7%) as females (35.3%) with the majority of infections between 2 to 11 years of age. This finding corresponded to the context of boys preferentially engaging in outdoor activities, shorter hair increasing infection vulnerability, in addition to this age-group interacting more with pets (Findlay, 1974). Poor caregiver knowledge about hygiene practices, such as the lack of sanitizing hair-grooming utensils shared between children, propagates spreading this contagious infection (Ayanlowo, 2018). A steep reduction of these infections was seen in adolescent ages, correlating with heightened immune response at puberty (Findlay, 1974) by means of secretion of more sebum-containing fungicidal fatty acids (Ayanlowo, 2018).

5.2.2 Infections in Africa and other countries

African studies showed a predominance of infections with overall prevalence showing up to four-fold higher values compared to Johannesburg. Fungal infections were most common in Lagos (Ayanlowo, 2018) and North Tanzania (Kiprono, 2015), bacterial infections mostly seen in Southern Ethiopia (Kelbore, 2019), and ectoparasitic infections were overwhelmingly prevalent in rural Tanzania (49.4%) (Gibbs, 1996). Attributable causes that facilitate skin infections included weather conditions of high temperature and humidity, combined with overcrowded living conditions, restricted water access and poor hygiene habits (WHO, 2005).

Variations regarding proportion of atopic dermatitis and infections was seen in Sub-Sahara African reports. The study from Lagos (Ayanlowo, 2018) portrayed a categorically high prevalence of infestations and other infections at 13.6% and 26.1% respectively. Significantly, atopic dermatitis had a prevalence of 24.9%, and was the most common individual diagnosis in the study, which was indicative of an increasing burden of this disease in Nigeria (Ayanlowo, 2018).

Southern Ethiopia (Kelbore, 2019) had higher prevalence of infectious skin diseases such as impetigo (13.8%) and tinea capitis (12.7%), followed by atopic dermatitis (11.3%). As was also seen in Nigeria, the parasitic infections (9.6%) ranked within

the top four most common categories. These figures were significantly higher than South African values which decreased from 2.8% in 1974 (Findlay, 1974), to 0.7% in 2016 (Katibi, 2016) and now at 0.45%. This could be due to improved identification and efficient management of these conditions from a primary level of care. This therefore would validate the implementation of an interventions in neighbouring African countries, modelling successful examples seen in South Africa such as EDL guidelines for primary health-care.

A Tanzanian study by Gibbs in 1996 showed a heavy burden of infection-related skin disorders within a rural environment. His results showed that 73.9% of all cases comprised of transmissible skin diseases and only 26.1% were non-transmissible. 49.4% of all cases presented with ectoparasite infections. Atopic dermatitis was described to be rare (0.6%) in this village population in the northwest part of the country.

The profile of common skin conditions differed in a tertiary hospital in northern Tanzania. Dermatitis affected 34.1% of children followed by fungal (22.6%) and bacterial (13.2%) infections (Kiprono, 2015). A seven-fold lower infestation prevalence was seen (7.4%) compared to the rural study.

Contrasting statistics from nearby regions within the same country indicated the impact conveyed by living conditions and environmental factors on skin infection patterns. In addition, it showed that the proportion of conditions seen at a single location is not fully representative of a whole community. High household density was significantly related to transmissible skin disease in rural Ethiopia (Gibbs, 1996). Within poor socioeconomic settings, overcrowded housing conditions and poor hygiene practices foresee high scabies infection rates, and contaminated water sources favour pyoderma infections (Gibbs, 1996).

In South Africa the proportion of skin infections (5.03%) was similar to those in China (5.66%) (Hon, 2004). The Swiss result of 13.4% doubled in comparison, with a high viral infection component (10%) (Wenk, 2003). These all shared in common a predominance of viral rather than bacterial, parasitic or fungal infections typically seen in Sub-Saharan African studies.

Infections ranked in first two most prevalent conditions in all African studies reviewed. Apart from viral infections, which ranked within the top 3 conditions in China and Switzerland, remaining infections were significantly less prevalent with China showing tinea infections to be 9th most common diagnosis in the study group (Hon, 2004) with bacterial and fungal infections representing the 7th and 11th prevalence rankings respectively in Switzerland (Wenk, 2003). Dermatophyte infections were 3rd most common at CMJAH (2.82%), was most prevalent in Nigeria (16.3%) and the second most commonly seen diagnoses in Southern Ethiopia (18.8%) (Kelbore, 2019) and Northern Tanzanian regions (22.6%) (Kiprono, 2015).

It could be implied that South Africa shows a relatively better socio-economic profile compared to nearby African countries in that a smaller prevalence of infestations and infectious diseases represent better living conditions such as less overcrowding, better access to health-care and treatment availability.

Comparisons between first world and developing nations highlighted the need for different populations to prioritize a targeted intervention for skin diseases according to specific needs. Skin diseases were hereby shown not to be universally equal. Resource-poor areas in Africa would benefit from interventions aimed at reducing health-care obstacles by way of promoting awareness and knowledge about endemic skin conditions, and improving access to medical care (Hay, 2011).

5.3 Pigmentary disorders

Pigmentary disorders represented the third most common category in the current study, with vitiligo and albinism having represented the majority of these.

Vitiligo was the fourth most common individual diagnosis made in the current study at CMJAH (2.1%), with consistent age group representation from 2 to 18 years of age. A fourth highest ranking was also seen in Durban in 2016 with a higher prevalence of 4.1% (Katibi, 2016). Vitiligo ranked within the ten most common diagnoses in many of the reviewed African studies, including Nigeria (3.2%), Ethiopia (3.6%) and Tanzania (2.9), showing similar prevalence throughout.

Albinism had a much lower prevalence of 0.62% at CMJAH, which was half the proportion seen in Durban (1.2%) (Katibi, 2016). The severity of possible cutaneous and ocular complications due to this condition would anticipate the need for a higher number of patients presenting to a specialist skin clinic. As this genetic disorder is visible from birth, patients of all ages would be expected to be examined, with longitudinal surveillance for photodamage and malignancies. Such visits would benefit these patients by providing sunscreens and emphasising sun protection measures (James, 2020c). Such expectations were not realised in the overall data comparisons. Hong et al (2006) described many obstacles to health provision, including patient isolation due to being stigmatized in society, uneducated about their condition and associated complications, combined with shortcomings of healthcare initiatives not actively addressing this disorder, along with insufficient resources such as sunscreens to do so (Hong, 2006). Consequently, as was documented in an epidemiological study in Zimbabwe, only a minority of patients with albinism sought medical attention, with less than one quarter of these patients ever having a skin examination, and less than half having eye tests done (Franklin, 2018). Venter et al concluded an estimated prevalence of Albinism in the South Africa to be 1 in 2833 (Hong, 2006). Low prevalence documentation for this condition within specialist clinics in South Africa suggests the need for more proactive intervention strategies to enable easier healthcare provision to these patients. Tanzania showed the highest prevalence in the comparative studies. A higher proportion of these patients seen may be due to this country providing more proactive initiatives in addressing these patients, for example by way of mobile albinism skin clinics set up in villages (Hong, 2006), and creating more comfortable health-care environment.

5.4 Appendageal disorders

Acne vulgaris was most commonly seen in adolescents with a six-fold increase in case numbers compared to 6–11year old age group, showing an almost equal female-male ratio of 58%:42%. This finding was expected as the onset of acne is attributed to the rise of androgen hormones in teenage years (James, 2020a). It was found that 52% of these adolescent patients had acne in addition to a second skin condition, whereby in 73% of these cases, was atopic dermatitis. This finding could

partly explain an unusually high prevalence of atopic dermatitis in this clinic, whereby patients with a history of atopic dermatitis developing acne vulgaris remain in the clinic system for longer. These patients are still classified as having atopic dermatitis with acne added to the assessment list, regardless of this possibly being controlled and possibly resolved. Another interpretation may be that many adolescents with acne vulgaris are being treated at initial presentation by general practitioners with fewer referrals made to the specialist clinic.

Pre-pubertal acne was seen in 18% of all cases. One patient presented with acne neonatorum at 9 months of age. Such cases required follow up to ascertain the outcome of resolution due to waning of neonatal androgens, or alternatively warrant further investigation of organic causes if persistent thereafter (James, 2020a). Endocrinological pathologies that result in excess androgen production may be suspected if acne develops during 1 – 7 years of age (James, 2020a). Within the study group, CAH was a medical co-morbidity present in two of the five acne patients, both 8 years of age.

5.5 Vascular disorders

Infantile haemangiomas were only seen in the youngest age group. This was expected due to this condition presenting at birth, with lesions proliferating in the first 6 months of life, followed by involution. Growth after one year of life is rare (James, 2020b). The amount of these cases seen in this time period is likely under-reported as these cases are often consulted for in neonatal wards post-delivery rather than in the clinic. The eldest reported case was of a two-year old female. This was in keeping with an involuted haemangioma with redundant skin requiring further surgical referral.

5.6 Multiple skin diagnoses in the study group

5.73% of total study group had more than one skin condition. In South Africa this has previously been documented to be 15% in Pretoria (Findlay, 1974) and 9.8% in Durban (Katibi, 2016). The current study showed lower prevalence of multiple skin

conditions than in other regions such as Southern Ethiopia (8.2%) (Kelbore, 2019), in Northern Tanzania (16.5%) (Kiprono, 2015) and in China (10.9%) (Hon, 2004). In the current study atopic dermatitis represented the most common diagnosis that co-existed with another (in 79,2% of these patients). Other conditions mostly paired with atopic dermatitis included non-related pathologies such as dermatophyte infections (40.6%), acne vulgaris (12.5%), followed by closer-associated conditions of molluscum contagiosum (6.25%) and impetigo (5.21%). Few completely unrelated paired diagnoses were also seen such as psoriasis with acne vulgaris. A majority of adolescents with acne vulgaris also had atopic dermatitis (73.3%). The finding of multiple diagnoses emphasizes the importance of thorough skin examination by clinician at every visit to prevent overlooking new or unexpected skin pathology, and to be vigilant in finding changes that may be associated with an already present condition (Katibi, 2016).

5.7 Medical co-morbidities in the study population

The results of the study indicated that co-morbidities were only documented in 1% of the study group. The unexpectedly low proportion of cases failed to adequately represent significant associations between skin and other diseases within this patient group.

Low co-morbidity documentation in this study did reflect expected findings, such as those emphasized in the publications known as the EpiChron Cohort Study from Spain. This showed co-morbidities in 43% of 33 591 patients with atopic dermatitis (Gilaberte, 2020). Within the current study population showing a prevalence of atopic dermatitis, more cases of common associated co-morbidities such as asthma or allergic rhinitis in defining an ‘atopic march’ would be expected in these patients. At least one of these co-morbidities was seen in up to 80% of the EpiChron group (Gilaberte, 2020). Psychosocial disorders (7.9%) and visual impairment (7.8%) were also reported in up to 7.9% and 7.8% of these patients respectively (Gilaberte, 2020), which further impair the quality of life of these patients. Acute conditions including upper respiratory tract infections (54.4%), otitis media (12.8%), conjunctivitis (10.1%) and pharyngitis (7.9%) were also noted to occur more frequently in these children (Gilaberte, 2020).

Possible reasons for the unexpectedly low co-morbidity entries in the clinic included the following:

- Most patients were otherwise healthy and presented with isolated skin disease, and that negative findings of other co-morbidities were not listed
- Doctors' notes focused primarily on the description of skin-related signs and symptoms and omitted to document co-morbidities that are documented in different files at other respective clinics
- The absence of incorporated tick-sheets or clerking sheet sections to prompt a routine enquiry of specific co-morbid symptoms
- There may be a greater emphasis on finding out the HIV exposure or status of children, but not as much on other conditions generally which may seem relatively less significant or unnecessary in view of skin diseases
- Negative impacts on the patient and caregiver's mental health or lifestyle are not routinely documented. Such broader contexts of patient morbidity may not be considered a primary target of intervention in a specialist clinic setting, as is the need to treat the presenting physical skin pathology
- Language barriers may have had limitations as in such situations truncated information through translation, or acquiring it from summarized referral notes is likely.

The above practical drawbacks in the clinic may have cumulatively contributed to the paucity of documentation regarding co-morbid conditions in these patients.

6.0 LIMITATIONS

Limitations relating to the data collection process were experienced. Some of the patient files were not found within the alphabetized filing-cabinet arrangement. Some patient files were not found in the central dermatology filing drawers due to additional space needed to accommodate more files. This resulted in searching multiple storage containers for individual patients. In addition, some of the patient files had incomplete records after lost files needed to be replaced. This manual filing setup, and the absence of electronic databases capturing patient diagnostic information, affected the total number of patients seen, and may have influenced the proportions of some diagnoses seen over the duration of a year.

A drawback seen was the limited data obtained for medical co-morbidities in this study group. As this was a retrospective study, a directed approach to actively record positive and negative findings for all patients was not pre-empted. This study design also did not make use of formalised tools by which to formally identify symptoms defining common conditions, especially atopic dermatitis. Most diagnoses were made on a clinical basis, therefore portraying a possible degree of clinician-related subjectivity. Multiple follow-up visits of patients conveyed a repeated assessment of atopic dermatitis in the absence of clinical signs over prolonged durations. This may have resulted in a relative over-reporting of this conditions in cases that may have already resolved.

7.0 RECOMMENDATIONS

This prevalence study represented the first of its kind at the paediatric dermatology clinic at CMJAH in Johannesburg. This formed a basis from which further studies can be done. Identifying atopic dermatitis as a highly prevalent skin condition at this clinic encourages further studies around this topic. Important factors such as ethnicity, socio-economic status and migration trends, would identify risk factors that may contribute to onset of disease in this community.

Collaboration with molecular biologists in establishing a link between atopic dermatitis to specific genetic loci within the population group would enhance the understanding on the pathogenesis of this disease. Endeavours to calculate the cost- per- patient pertaining to treatment of the most common skin diseases, would facilitate budget distribution and prevent unnecessary spending by clinics and hospitals treating these patients.

Within an established specialist clinic setup, longitudinal prevalence follow-up studies would be useful in calculating the annual rate of atopic dermatitis. This would indicate effectiveness of current interventions, or alternatively alert the need for better management if the rate inclines.

In view of many patients in the specialist clinic being controlled on treatment and retained within the system over long durations, the documentation of new cases per year instead of all patients with the diagnosis would more reliably depict dynamic rate changes.

Future studies can look to successful, validated study models to base methods of data collection on. The ISAAC study principles and a prospective questionnaire-based approach would be a reliable guide with regards to atopic eczema studies. With a prospective study the incorporation of a structured approach amongst all doctors can be co-ordinated. In addition, standardised clerking sheets that prompt entry of co-morbidities can be used.

8.0 CONCLUSIONS

Very few prevalent studies of skin diseases in children have been done in South Africa. Skin disorders encompass a wide spectrum, however a select complement of conditions predominate within populations. Clinic-based studies are important to identify the particular disease burden in that setting, to allow for practical, targeted management implementation.

In this study, it was found that atopic dermatitis was significantly prevalent within the clinic at CMJAH. This correlated to worldwide data indicating this disorder to be a tremendous burden of disease. There has been a prevalence rise over the last 47 years according to previous studies done in South Africa. This therefore warrants further research on atopic dermatitis at this clinic to identify possible modifiable risk factors which could lead to the implementation of strategies aimed at reducing this burden over time. Findings showed a smaller proportion of infectious skin diseases relative to those compared in African clinics. This may indicate relatively effective identification and treatment at primary care level in South Africa. The lower infection component in conjunction with the increasing prevalence of atopic dermatitis represented a state of growing urbanisation in our community. This phenomenon may be imminent in surrounding African countries, as atopic dermatitis was prominent despite relatively higher infection ratios.

Prevalence trends showed variation between centres, geographic regions, and different countries, which suggested a dynamic interplay of environmental, socio-economic and molecular factors in the manifestation of skin pathology. By identifying the broad multifactorial impact of conditions such as atopic dermatitis on quality of life, it was concluded that future prevalence studies are needed to provide necessary solutions to life-changing diseases, with the intention to measure the progress rates and effects of such interventions over time. Large studies such as ISAAC highlight essential principles of consistent definition of diagnosis, and standardised approach in collecting information over time, and form a platform for smaller studies to emulate.

In view of this study being clinic-based and using retrospective data, the findings would be valuable for potential clinic-directed interventions, so benefiting this

population group. Possible outcomes from this study would be to motivate hospital management in supplying adequate ranges and quantity of treatment for common conditions such as atopic dermatitis. Providing prevalence data would assist in hospital budgeting efficiency, by reducing losses caused by unnecessary spending, and simultaneously guarantee provision of in needed medication to more patients. A proactive involvement of health-care workers the clinic would be essential. Educating caregivers and patients about atopic dermatitis and offering practical treatment advice is inexpensive and would contribute to the improvement on quality of life through holistic support.

APPENDIX A

DATA COLLECTION SHEET

AGE	GENDER	PRIMARY DIAGNOSIS (according to ICD-10 classification)	SECOND DIAGNOSIS (if applicable)	CO-MORBIDITIES

APPENDIX B

ETHICS APPROVAL CERTIFICATE

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R14/49 Dr Fotis Kouvelakis

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M191148

NAME: (Principal Investigator)	Dr Fotis Kouvelakis
DEPARTMENT:	Faculty of Health Sciences Charlotte Maxeke Johannesburg Academic Hospital Department of Dermatology (Dermatology Paediatric Clinic, Area 256)
PROJECT TITLE:	The prevalence and spectrum of skin disorders at the Paediatric Dermatology Outpatient Clinic of the Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) in Johannesburg, South Africa
DATE CONSIDERED:	29/11/2019
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Prof Deepak Modi
APPROVED BY:	Doctor CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	12/03/2020

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on the Third Floor, Faculty of Health Sciences, Phillip Tobias Building, 29 Princess of Wales Terrace, Parktown, 2193, University of the Witwatersrand. I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report**. The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. In this case, the study was initially reviewed in **November** and will therefore be due in the month of **November** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

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