CLINICAL PROFILE, TREATMENT AND OUTCOME OF CHILDREN WITH XERODERMA PIGMENTOSUM AT MUHIMBILI NATIONAL HOSPITAL, DAR ES SALAAM, TANZANIA.

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Mmed (Paediatrics and Child Health) Dissertation
Muhimbili University of Health and Allied Sciences
October 2021

Muhimbili University of Health and Allied Sciences
School of Medicine

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By

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A Dissertation Submitted in Partial Fulfillment of the Requirements for the Degree of Master of Medicine in Paeditrics and Child Health at

Muhimbili University of Health and Allied Sciences

October, 2021

CERTIFICATION

The undersigned certifies that, he has read and hereby recommends for examination by Muhimbili University of Health and Allied Sciences a dissertation entitled: ‘‘**Clinical profile, treatment and outcome of children with xeroderma pigmentosum at Muhimbili National Hospital, Dar es salaam, Tanzania”** in partial fulfillment of the requirements for the degree of Master of medicine in Paeditrics and Child Health at Muhimbili University of Health and Allied Sciences.

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Date: _____

DECLARATION AND COPYRIGHT

I, **Hajaj M Salum** declare that this, **dissertation** is my own original work and has not been accepted for a similar degree in any University.

Signature: ……. Date: ……

ACKNOWLEDGMENT

I would like to acknowledge the Almighty God for keeping me alive up to this moment and blessing me with the opportunity to present my dissertation.

I am also grateful to the constant support from Dr. Helga Naburi, my supervisor and my Co supervisor Dr Lulu Chirande who has guided and mentored me into finishing this research.

I am thankful to the MUHAS administration and Pediatrics department for their assistance in the making of this dissertation report.

I am grateful to the Department of Pediatrics at Muhimbili National Hospital (MNH) for allowing me to conduct this study.

Last but not least, I am very humbled by Dr Mubina, my wife`s contributions, encouragement and continuous moral support together with my family, my mother Ummukulthum Karama, for all the sacrifices they made on my behalf during this study period.

DEDICATION

This work is dedicated to my late father Mohamed Bahajaj for his dedication and unfailing devotion. May Allah grant him Jannah.

ABSTRACT

Introduction: Xeroderma Pigmentosum (XP) is a rare hereditary disease of defective deoxyribonucleic acid repair defined by extreme sensitivity to sunlight, resulting in sunburn, pigment changes in the skin and a greatly elevated incidence of skin cancers. Estimated prevalence is between 1 to 50 per million population. Mortality mainly occurred secondary to malignancy from 2nd decade of life.

Objectives: To determine Clinical profile, treatment and outcome of children with xeroderma pigmentosum at Muhimbili National Hospital, Dar es salaam, Tanzania from June 2011 to December 2020.

Methods: A retrospective cohort study with a longitudinal follow up of the pediatric patients with XP who attended either the pediatric oncology unit or dermatology clinic at MNH. A total of 100 files and database records of registered patients with XP were extracted using a structured data collection tool. All patients with available contact information identified in their case notes or database were contacted and consented for a short mobile interview. Data analysis was done using Statistical Package for the Social Sciences version 23. Patients' socio-demographical and clinical profiles were described using frequencies and percentages for categorical variables, for continuous variables means and standard deviations was calculated. Kaplan-Meier survival analysis was used to determine the overall survival rate of XP patients. Independent predictors of XP patients' survival were assessed in adjusted Cox regression model. The risk of mortality was presented using hazard ratio and 95% confidence interval and *P-value* less than 0.05 were considered as significant.

Results: Of the 100 enrolled patients, half were male. The mean age was 5.4 ± 4.1 years. Thirty six percent (36%) had family history of XP while only 8% had history of consanguinity. The mean age at first symptom presentation was 1.1±SD 1.8 years. Cutaneous manifestation was found in 99% of the patients, in which 41% had cutaneous squamous cell carcinoma (cSCC). Ninety three percent had ocular findings in which 25%

had developed ocular squamous cell carcinoma. Only 14% of XP patients had documented oral Squamous cell carcinoma. Surgical therapy, chemotherapy and radiotherapy were received by 54%, 31% and 25% respectively. At the end of the study follow up period, 39% of enrolled patients were alive and still on active follow up, while 35% of patients had been lost to follow up and death had been confirmed among 26%. The median survival was 14.1 years (IQR= 11.7 – 17.2). Estimated overall survival rate was 90%, 64% and 46% at 5, 10 and 15 years respectively. Those with cSCC had lower survival rate, 87% and 55% at 5 and 10 years respectively. Cutaneous squamous cell carcinoma was found to be a strong predictor of mortality among patients with XP (HR 2.8, 95% CI 1.0-7.3, *P*= 0.02).

Conclusion: Xeroderma Pigmentosum is an inherited disease which affects male and female equally. Skin and eyes are the most affected organs and can be protected by using protective measures such as sun cream and hats. Survival of the patients with XP is progressively decreasing from 90%, 64% and 46% at 5, 10 and 15 years respectively. Those XP patients with cSCC had lower survival rate compared to those with no cSCC which was found to an only predictor of mortality in patients with XP. We recommend early identification of patients with XP and initiation of preventive measures to reduce morbidity and mortality. This can be achieved by raising awareness among health care workers and the community, and by educating parents of patients with XP regarding the prevention of cSCC.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

ABBREVIATIONS

aHR	Adjusted Hazard Ratio
AR	Autosomal recessive
CI	Confidence Interval
cSCC	Cutaneous Squamous cell carcinoma
DNA	Deoxyribonucleic acid
HB	Haemoglobin
HR	Hazard Ratio
IQR	Interquartile range
MNH	Muhimbili National Hospital
NER	Nucleotide Excision repair
NMSC	Non-melanoma skin cancer
ORCI	Ocean Road Cancer Institute
OS	Overall Survival
POC	People of skin color
SCC	Squamous cell carcinoma
SD	Standard deviation
SPSS	Statistical Package for the Social Sciences
UV	Ultraviolet
UVR	Ultraviolet radiation
USA	United States of America
XP	Xeroderma Pigmentosum
XPA	Xeroderma Pigmentosum subgroup A
XPD	Xeroderma Pigmentosum subgroup D
XPG	Xeroderma Pigmentosum subgroup G
XPV	Xeroderma Pigmentosum variant

DEFINITION OF TERMS

Survival rate: The proportion of patients diagnosed with XP who were or are still alive from the time of diagnosis.

Disease Status: Current condition of the patient, whether is improving, worsening or remained the same as perceived by parent/guardian.

Lost to follow up: Patients who could not be found on phone and their last clinic follow up is more than 3 months from the date of data collection

1.0 INTRODUCTION

1.1 Background

Hereditary diseases are group of diseases caused by genetic mutations that are inherited from a parent's genome. They can be caused by a mutation in one gene, mutations in multiple genes, a combination of gene mutations and environmental factors, or damage to chromosomes.

Xeroderma Pigmentosum (XP), is a rare recessively transmitted hereditary disease with 100 percent penetrance due to a defect in nucleotide excision repair of deoxyribonucleic acid (DNA). Damage in skin cells associated with exposure to sunlight is characterized by extreme sensitivity to sunlight, resulting in sunburn, pigment changes in the skin and a high incidence of skin cancers (1). Xeroderma Pigmentosum is caused by mutations in any of eight genes involved in the recognition and repair of ultraviolet radiation (UVR)-induced DNA damage in a pathway called nucleotide excision repair (NER). Based upon the specific gene affected, XP can be divided into seven XP subgroups or complementation groups, Xeroderma Pigmentosum subgroup A (XPA) through G (XPG), and Xeroderma Pigmentosum variant (XPV) (2).

Xeroderma Pigmentosum has been found in all continents and across all racial groups. It is found in equal prevalence in males and females consistent with autosomal recessive (AR) inheritance. Geographical distribution contributes to the observed variable incidence and prevalence. Estimated prevalence is 1 per million population in United States of America (USA) (3), 2-3 per million population in Europe (4), 20 per million pollution in Africa (5) and reaches up to 50 per million population in Japan (4).

Xeroderma Pigmentosum present as early as the first weeks of life in 60% of the patients who present with sun sensitivity manifested by pain and easy sun burning. The remaining 40 percent present in childhood period with an unusually increased number of lentigines in sun exposed areas like nose, zygoma and forehead and then appear on the sides of the neck, mostly sparing the area under the chin. Without rigorous sun protection, the skin undergoes several changes resulting in areas of hyper and hypopigmentation followed by

in-situ melanocyte and keratinocyte malignancy, and eventually multiple basal cell carcinomas, invasive squamous cell carcinoma (SCC) and melanomas. Xeroderma Pigmentosum patients have a 10, 000-fold increased risk of non-melanoma skin cancer and a 2,000-fold increased risk of melanoma under the age of 20 (1,6).

Eyes are involved as frequent as skin but limited to UVR-exposed structures of the eye. Photophobia is often present and may be associated with prominent conjunctival injection. Continued sunlight exposure may result in severe keratitis, leading to corneal opacification and vascularization, and neoplasms .(7)

Oral and neurological abnormalities are also not uncommon in XP. Patients develop cancers of oral cavity at tip of the tongue, a presumed sun-exposed area. The neurological abnormalities are the result of progressive neuronal degeneration resulting in sensorineural deafness, ataxia, areflexia, microcephaly and intellectual deficiency as well as impaired eyesight (1).

The diagnosis of XP is made on the basis of clinical findings and family history. The confirmation of XP diagnosis is done by several studies including cellular hypersensitivity to UVR, chromosomal breakage studies, complementation studies and gene sequencing studies to identify the specific gene complementation group (3).

Careful avoidance of sun exposure (UVR) combined with chemoprevention of skin cancer and surgical treatment of precancerous and cancerous cutaneous, ocular and oral lesions as they arise, have been the mainstay of traditional treatment of XP (8).

Patients with Xeroderma Pigmentosum have less survival rates compared to general population. Death mainly occurs from the 2nd decade of life. Those with skin cancer and neurologic degeneration have the poorest survival rates and have been reported to be the most common cause of death among XP patients (6)

1.2 Literature Review

1.1.2 Epidemiology

Xeroderma Pigmentosum is a very rare hereditary condition of defective DNA repair following sun ultraviolet light exposure. It affects all races worldwide with observed disparity in prevalence and incidence. Studies done in different countries including high, middle and low income countries have shown the variation in its prevalence, ranging from 1 per million population to 50 per million (4,9).

In USA, the prevalence of XP is estimated to be 1 per million population, while it is reported to be relatively higher in Europe reaching up to 2 to 3 per million. This could have been contributed by a number of immigrants coming from North Africa, East Europe and Southern of Asia, areas with high frequency of the disease (4,10).

The burden of the disease is found to be high in Asia, heavily contributed by the high level of consanguineous marriages in the region. The estimated prevalence in Japan ranges between 1 to 50 per million population (4,11) while it is relatively lower in Pakistan but still higher compared to that of USA and Europe (12).

In Africa, the disease was mostly studied in patients from Northern countries including Libya and Morocco, The incidence in Libya was reported to be between 15-20 million per population (5,9). An almost similar incidence was found in Morocco (13).

Although fair number of patients have been seen in our setting, apart from 1 case report explaining 2 different patients developing 2 different malignancies simultaneously in Zanzibar, no other data regarding the disease has been published (14).

1.2.2 Social demographical profile

Xeroderma pigmentosum is a rare AR disorder that results from a defect in NER (1). It is a hereditary condition which runs through families and is passed from one generation to another. Two copies of an abnormal gene must be present to develop the disease. The risk of the disease increases with consanguinity. Up to 90 % of the patients with XP reported from Africa are product of consanguineous marriages (5).

Area of residence plays an important role in the development of the symptoms of XP. The symptoms are thought to have a close relationship with the latitude and weather (15). However, defective repair of DNA damaged by UVR plays a key role in the pathogenesis of XP. Sunny climates exacerbate the cutaneous features, resulting in multiple pigmentation changes, multiple skin cancers and early death. Nonmelanoma skin cancer is clearly linked to sun exposure, as it is found in greatest frequency in regions nearest to the equator (15). Patients from Africa showed to have developed malignancies more and in a very young age compared to those from Europe and America (5,16).

Onset of sign and symptoms of XP vary with the age of the patient. Those who have extreme sunlight sensitivity present in a very young age, as early as in infant period which takes many days or weeks to resolve (1). Conversely, those who do not show any sunburn reaction as their first manifestation, symptoms often occurs by two years of age, unusually increased number of lentigines (freckle-like pigmentation) in sun exposed areas (1).

In our setting, knowledge regarding social-demographical profile of patients with XP is lacking, including their age at presentation, common complications and survival. Thus this study aimed to uncover this information

1.2.3 Clinical Profile

The onset of XP presentation is of acute onset in approximately 60% of the patients who present with sun burn as their first manifestation. The other 40% of cases do not show any sunburn reaction have more gradual onset of the symptoms. The presenting symptoms and signs are mainly caused by inability of DNA repair in areas exposed to sun ultraviolet (UV) light (1). The most common symptoms are sunburns, blistering, photosensitivity, hypo and hyper-pigmentation, freckling and premature aging, lentiginosis, actinickeratosis followed by SCC, basal cell carcinoma or melanoma in the absence of rigorous protection from the sun (17).

Ocular abnormalities are almost as common as the cutaneous abnormalities, but they are strikingly limited to the anterior, UVR-exposed structures of the eye (lids, cornea, and conjunctiva). Photophobia is often present and may be associated with prominent conjunctival injection. Persistent exposure to sunlight may result in severe keratitis, leading to corneal opacification and vascularization, and in neoplasms (epithelioma, squamous cell carcinoma, and melanoma (1). Other organs are involved less frequently include oral cavity and central nervous system.

A retrospective study done in Turkey between 2004 to 2010 which analyzed XP patient's clinical profile showed that the most clinical presentations were pigmented macules (100%), actinic keratoses, keratoacanthoma, facial skin ulcer (20%) while 40% of the patients had skin malignancy. Ocular involvement was seen in all patients, 60% presented with conjunctivitis, 40% with photophobia, while ectropion, glaucoma, conjunctivitis, SCC at upper left eyelid, blepharitis were seen in less than 1% each (16).

The most common presentations of 36 XP patients studied in Pakistan between 1995 to 2001 were burning of skin and freckles in 100% of the patients, while 43% of the patients had actinic keratosis, 22 % had keratoacanthoma, 11% had face ulcer and 17% had developed skin malignancies. Ninety percent of the patients had ocular involvement mostly photophobia and conjunctivitis while other findings like corneal keratitis and lid ulcer present in less than 40% (12).

The occurrence of common clinical symptoms pointed out in a retrospective study conducted in Libya were multiple freckles and hypopigmented macules (100%), actinic keratosis (83%), keratoacanthoma (16%). Malignant growth observed were SCC in 63% patients, basal cell carcinoma in 50%, and basosquamous carcinoma in 8%. Photophobia presented in 95 % of the patients (9). There is scarcity of information regarding clinical profile of patients who live in sub- Saharan African. This is reported in this study.

1.2.4 Treatment Modalities

Gene therapy is the ideal goal for curing XP, but there are many hurdles to be crossed before this ideal becomes a reality. The approach offers long-term hope for XP cures, but currently, complete protection from solar UVR (use sunscreen, sun-protective clothing, sunglasses, and UV-protective goggles) is by far the best strategy for cancer avoidance. The management of patients with XP requires a multidisciplinary team including dermatologists, ophthalmologists, oral surgeons, genetics professionals, and neurologists. Strict sun protection and avoidance, close clinical follow-up with regular skin and eye examination, and appropriate and early management of any premalignant and malignant skin lesions are the mainstays of treatment (8).

Early rigorous protection from UV light reduces the incidence of developing skin malignancy (1) but due to increased frequency of malignancy in XP patients, chemoprevention applied to the sun exposed area is effective in preventing skin cancer of exposed sites. Systemic retinoids given at high doses have been used for chemoprevention of non-melanoma skin cancer (NMSC) in patients with XP. It helps to prevent skin cancer through modulation of cell proliferation, differentiation, and apoptosis (18). Topical fluorouracil and imiquimod, antineoplastic drugs have also been used (8).

Once the malignancy develops, surgical excision becomes the treatment of choice. Due to the high number of tumors that may occur in neighboring sites, wide surgical margin has been replaced by a modernized narrow margins surgical excision. The former used to leave large defects in areas with no skin due to previous surgeries. This resulted in confusion between sites of inadequately treated skin cancer and defects due to surgery. In addition, wide excisions did not prevent the development of new tumors in the same field (8).

Too often the least developed countries including ours remain behind in terms of availability of advanced equipment and medication. The acquired facts from this study will help us understand what treatment modalities are available and are received by our patients diagnosed with XP at our setting.

1.2.5 Outcome (Survival Rate)

Survival of patients with XP has been understudied despite various case studies and case series reporting a significant number of death of patients with the disease. At present, little to none is known regarding their survival time and risk factors affecting the survival. Patients with XP have 10000-fold risk of developing cutaneous squamous cell carcinoma (cSCC) before the age of 10, which is reported to be the leading cause of death of these patients starting from the 2nd decade of life. Since cSCC occurs mostly in the 4th decade of life in general population, many of the studies are around this age group. Five-year survival rate of patients with cSCC ranges between 42-90% (1,19–25).

In USA, A 3-year survival rate of patients with cSCC was found to be 100% in patients with no risk factors but only 70% with patients with at least one risk factor, while 5-year survival rate of patients with cSCC was reported to be 90% for those with stage 1 while decreasing significantly to 75 and 42 % for stage 2 and 3 respectively (23,24).

In Europe, a prospective study which was done in Germany found a 3-year survival rate of 65.5 %. This unfavorable low survival rate could be attributed by an increase in the median age of the patients and associated comorbidities compared to those reported before (25).

A study done in Romania reported a 5-survival rate of 86% in men and 100% in women with early disease while significantly dropping to 55% in men and 19% in women with advanced stage, almost similar to the findings reported in Germany and USA.

Comparable findings were reported in Finland, Sweden and Norway with a 5-year survival rate of 90%, 88%, and 87% respectively (19–22). At present little is known about the survival of the patients with XP in Africa, the acquired information from this study aimed to close the knowledge gap.

1.2.6 Mortality risk factors

Since XP is a very rare disease, current literature review lack studies directly looking at risk factors affecting survival of patients with XP, although many descriptive studies reported a significant number of deaths are secondary to skin cancer followed by neurologic degeneration which are the complications of the disease (1,5,12).

Cutaneous skin cancer

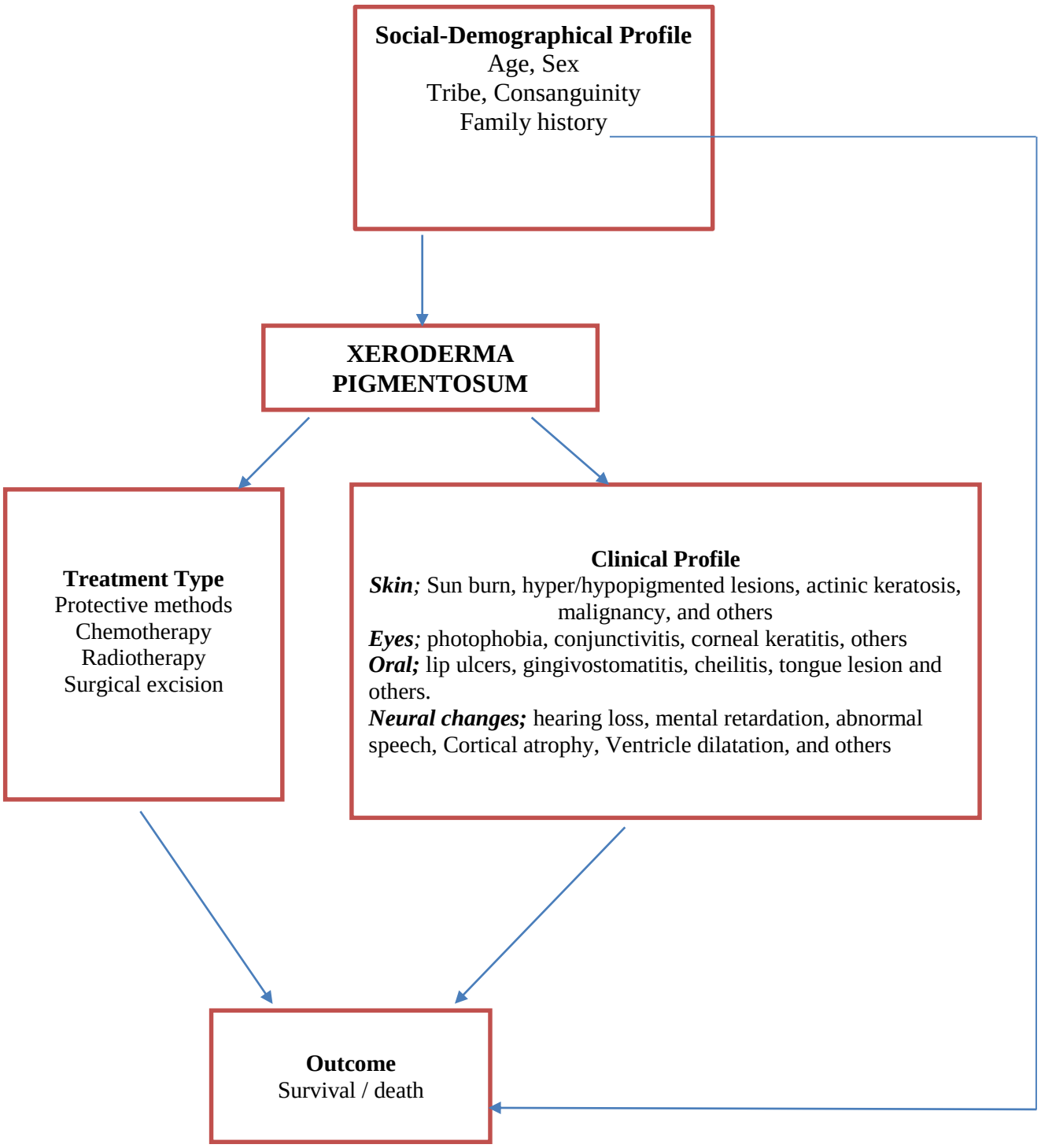
Patients with XP have 2000-fold risk of developing melanoma skin cancer and 10000-fold of NMSC. The most common NMSC developed by these patients is cSCC which predispose the patient to low immunity. Several studies reported cSCC to be the leading cause of death in these patients. In a 40 year follow up study of 106 patients with XP in USA, 34% of the death were attributed to skin cancer while in 7-year study done in Pakistan, 2 out of six patient who developed skin cancer died before age of 10 (1,6,12).

Neurologic degeneration

Approximately 30% of the patients with XP develop neurologic degeneration; hearing loss, mental retardation, feeding problems, abnormal speech, cortical atrophy, ventricle dilatation. This is 2$^{nd\ most}$ common cause of death in these patients following skin cancer. In a 40 year follow up study of 106 patients with XP in USA, 31% of the death were due to skin cancer. The median age at death in XP patients with neurological degeneration was significantly lower than those XP patients without neurological degeneration ($p=0.02$) (1,6). As previously stated, due to the scarcity of information regarding risk factors, this knowledge gap was closed by the information provided by this study.

1.3 Conceptual Framework

This conceptual framework shows how the outcome is determined by social-demographical profile, clinical profile and treatment type received by the patient.



1.4 Problem Statement

Xeroderma pigmentosum is a rare autosomal recessive (AR), neuro-cutaneous disorder related to DNA repair defects. Despite being a rare disease, about 30% of people with the disease develop progressive neurological abnormalities in addition to problems involving the skin and eyes. Furthermore, about half of patients with XP may develop their first skin cancer by age 10 (1).

Xeroderma pigmentosum has been found in all continents and racial groups. Estimated prevalence varies from as low as 1 per million population, to as high as 50 per million population (1). XP presents early in childhood following sun exposure. The early symptoms include sun burn reactions such as erythema, edema and vesicles.

Xeroderma pigmentosum is usually diagnosed by its typical clinical presentation, which is feasible in our setting. Although no cure is available for XP and gene therapy for definitive treatment of XP is still in experimental stages, patients who are diagnosed early and carry out lifelong stringent protection measures (complete protection from exposure to UV) the prognosis is good.

Mortality of the patients with XP is mainly secondary to SCC. The 5-year survival rate of patients with XP and SCC ranges between 42-90%, the difference is mainly due to difference in stage of the cancer with advanced disease carrying the lowest survival rate. (19–25). Furthermore, other factors contributing to mortality include, age, sex, hearing loss, mental retardation, abnormal speech, cortical atrophy, ventricular dilatation, lip cancer, conjunctival malignancy, basal cell carcinoma and treatment modalities (6).

Despite having a fair number of patients presenting with XP in our facilities, data is limited with regard to their clinical profile and outcomes, which could help in prioritizing the patients when presents in early stages of the disease. Thus, this retrospective review study explored this aspect to fill the existing knowledge gap.

1.4 Rationale

This study aimed to shed light on the clinical profile, treatment and outcome of patients with XP in Tanzania and factors associated with the outcome from the time diagnosis. Furthermore, findings from this study are expected to help us to understand the pattern of distribution of the disease; such as where do most of our patients come from, common presentation and age of presentation, stage of disease at presentation, common complications of the disease (in our patients) and treatment modalities given to our patients. Findings of this study are expected to assist to raise awareness of health care workers in different levels to prioritize care including health education at first contact with the patient based on their risk factors so as to improve their quality of care, prevent complications and hence improve the outcome.

1.5 Research question

1.5.1 Overall Research question:

What is clinical profile, treatment and outcome of children with xeroderma pigmentosum at Muhimbili National Hospital, Dar es salaam, Tanzania?

1.5.1 Research questions

1. What is the socio-demographical profile of patients with XP at MNH?
2. What is the clinical profile of patients with XP at MNH?
3. What are the types of treatment received by patients with XP at MNH?
4. What is the survival rate of patients with XP from the time of diagnosis at MNH?
5. What are the factors associated with survival among patients with XP during the study period?

1.6.1 Objectives

1.6.2 Broad objective

To determine clinical profile, treatment and outcome of children with xeroderma pigmentosum at Muhimbili National Hospital, Dar es salaam, Tanzania from June 2011 to December 2020

1.6.3 Specific objectives

1. To determine the socio-demographical profile of patients with XP at MNH.
2. To determine the clinical profile of patients with XP at MNH?
3. To describe the type of treatment received by patients with XP at MNH?
4. To determine the survival rate of patients with XP at MNH.
5. To determine factors associated with survival among patients with XP during the study period

2.0 RESEARCH METHODOLOGY

2.1 Study Design

A retrospective cohort study with a longitudinal follow up

2.2 Study Duration

The study was conducted from March to April 2021.

2.3 Study Area

The study was conducted at the paediatric oncology unit and dermatology clinic at MNH in Dar es Salaam, Tanzania. MNH is one of the four tertiary hospitals in Tanzania.

The pediatric oncology unit was established at MNH in April 2011, after shifting from the Ocean Road Cancer Institute (ORCI). There are inpatient and outpatient services. The outpatient clinics attend to new patients as well as follow up patients. It receives about 500 new patients each year referred from all over the country. The unit has a capacity of 96 beds. The staff consists of oncologists, pediatricians, medical officers, residents and nurses. When need arise, the unit is free to consult different specialties which are available at MNH including ophthalmology, neurology, pediatric surgery, dental surgery, pathologist and others.

Dermatology department has established a dedicated pediatric dermatology clinic from 2014. The clinic gives services to new and follow up patients. It receives about 250 new patients each year. The clinics are attended by the dermatologists and dermatologic residents. Like Oncology unit, it can access the services of other specialties available at MNH via consultation.

Both units receive patients with xeroderma pigmentosum attending the hospital. Those who come with milder signs and symptoms usually seen at dermatology clinic while those with severe symptoms and signs of XP, including premalignant and malignant lesions usually referred to oncology unit.

2.4 Study Population

All patients diagnosed with Xeroderma pigmentosum who received services in the Pediatric Oncology Unit or Dermatology clinic from June 2011 to December 2020.

2.4.1 Inclusion criteria

a) All patients under 18 years of age at the time of diagnosis of Xeroderma Pigmentosum attended at Pediatric Oncology Unit or Dermatology clinic of MNH from June 2011 to December 2020.

2.4.2 Exclusion Criteria

b) Patients whose medical records missed important details were excluded.

2.5 Sample size calculation and selection

Convenient sampling technique was used to obtain the files of the participants until the minimum required sample size was achieved

Between June 2011 and Dec 2020, 120 patients were diagnosed with XP at MNH. The proportion of patients who dies from XP in our setting or other settings similar to ours is not known, Therefore, for the sample size calculation using adjusted formula for finite population size and p as 50% was as below; (26)

$$n_c = \frac{NZ^2pq}{\varepsilon^2(N-1)+Z^2pq}$$

Where by

N = finite population size 120

Z = level of confidence (1.96 for 95% confidence level) P = mortality rate (50%)
ℇ = margin of error 5%

$$nc = \frac{120 \text{ X } 1.96^2 \text{X } 0.5 \text{ X } 0.5}{0.05^2 \text{ X } (120-1) + 1.962 \text{ X } 0.5 \text{ X} 0.5}$$

$$= 90$$

With addition of a 10% non-response rate. The minimum sample size was 100 patients.

2.6 Data collection

All patients with the diagnosis of Xeroderma Pigmentosum who were treated at MNH (at both Paeditric oncology unit or/and Dermatology clinic) between June 2011 to December 2020 were identified by the investigator through the registry books or/and database in the paediatric oncology unit and Dermatology Clinic, and all were included in the study. Their case notes were traced using their registration numbers and a list of possible participants including their phone numbers was noted. Data was collected from participants' case notes and was recorded into clinical research forms (CRF) using a structured data extraction tool. Information collected included age, sex, family history, clinical presentation, treatment modalities and outcome.

All patients with available contact information identified in their case notes or database, and their status indicated as alive in the last hospital contact was contacted and consent for a short mobile interview. Those who consented were also asked about the well-being of the child including the disease status; stable, progressive or improving. If the child deceased after the last hospital contact, the date of death and whether the child died in hospital or at home was sought. For those who were not available through phone, their last visit within three months from the date of data collection was considered as their current disease status.

Pretest data extraction was conducted to check for completeness of the variables of interest and ensuring that the questions, which had been written in questionnaire, could be answered from this database. The necessary modification of questions was checked if there was any area where the questions confused or misled in order to ensure data quality.

2.5 Data Management

The data collected from the field was crosschecked by the principal investigator in order to remove errors. The data entry process was followed after completion of data collection activity. Several quality safeguards were incorporated into the data entry program. Once data was transferred into Statistical Package for the Social Sciences (SPSS) database, all questionnaires were reviewed again to ensure accuracy of data entry.

2.6 Study variables

Dependent variables; Dependent variable is the survival time measured from date of diagnosis to the date of death or alive at the time of data collection.

Independent variables

1. *Social-Demographical Profile;* Age, Sex, Tribe, Consanguinity, Family history
2. *Clinical Profile*

Skin; Sun burn, skin hyper/hypopigmentation, actinic keratosis, malignancy, others

Eyes; photophobia, conjunctivitis, corneal keratitis, Cataract, malignancy, others

Oral; erosion, gingivostomatitis, gum papilloma, cheilitis, tongue lesions (erosions, papillomas, hemangiomas, malignancy) and others.

Neural changes; hearing loss, mental retardation, Feeding problems, abnormal speech, Cortical atrophy, Ventricle dilatation.

3. *Treatment Type*

Pre-malignancy treatment; sun protective methods and chemoprevention of skin cancer

Malignancy treatment; Chemotherapy, Radiotherapy, Surgical excision

2.7 Data Analysis

Data cleaning and analysis was done using Statistical Package for the Social Sciences (SPSS) version 23. Socio-demographical profile, clinical findings and treatment modalities were described using frequencies and percentages for categorical variables and means and standard deviations for continuous variables.

Kaplan-Meier curves were used to estimate the Overall Survival (OS). The log-rank test was used to estimate differences in survival groups. Cox regression analysis was performed to examine if any factors were associated with mortality. Factors associated with mortality in the univariate analysis with *p-value* ≤ 0.2 were entered in multivariate analysis to identify and quantify predictors of deaths while controlling for potential confounder. Results are reported as adjusted Hazard ratio, 95%CI and p values for each variable included in the final model. For all analysis $p<0.05$ was considered statistically significant.

3.0 ETHICAL CLEARANCE AND ETHICAL CONSIDERATIONS

Ethical clearance numbered MUHAS-REC-2021-518 was sought from the MUHAS Directorate of research and publication, Institution Review Board (IRB). The permission to conduct this study was obtained from the directorate of research and publication MNH. Verbal consent was sought from patients or caregivers during the interview and they were informed on their right to participate and/or withdraw at any point from the interview.

Strict confidentiality was maintained, identification of participants was done by using number and assigned letters. Names of participants were not used at any point or appeared in the study. Furthermore, all the study documents were protected in a locked cabinet (paper based) and password protected computer files and these were only accessible to the investigators of this study. The exposure of the parents to the questions in the interviews could have led to psychological repercussions that were mitigated through immediate cessation of the interviews and continued only when parents were opted to do so. Those who needed medical help or had other children with same signs and symptoms of XP were advised to visit the hospital.

4.0 RESULTS

The study was conducted at the MNH Pediatric oncology unit and Dermatology clinic in Dar es Salaam. A total of 120 patients clinically diagnosed with Xeroderma Pigmentosum between June 2011 to December 2020 were identified from the hospital admission, clinic registry book and/or hospital database. We excluded twenty (20) patients whose files were missing. The remaining 100 patients were included in the final analysis as portrayed in Figure 1 below.

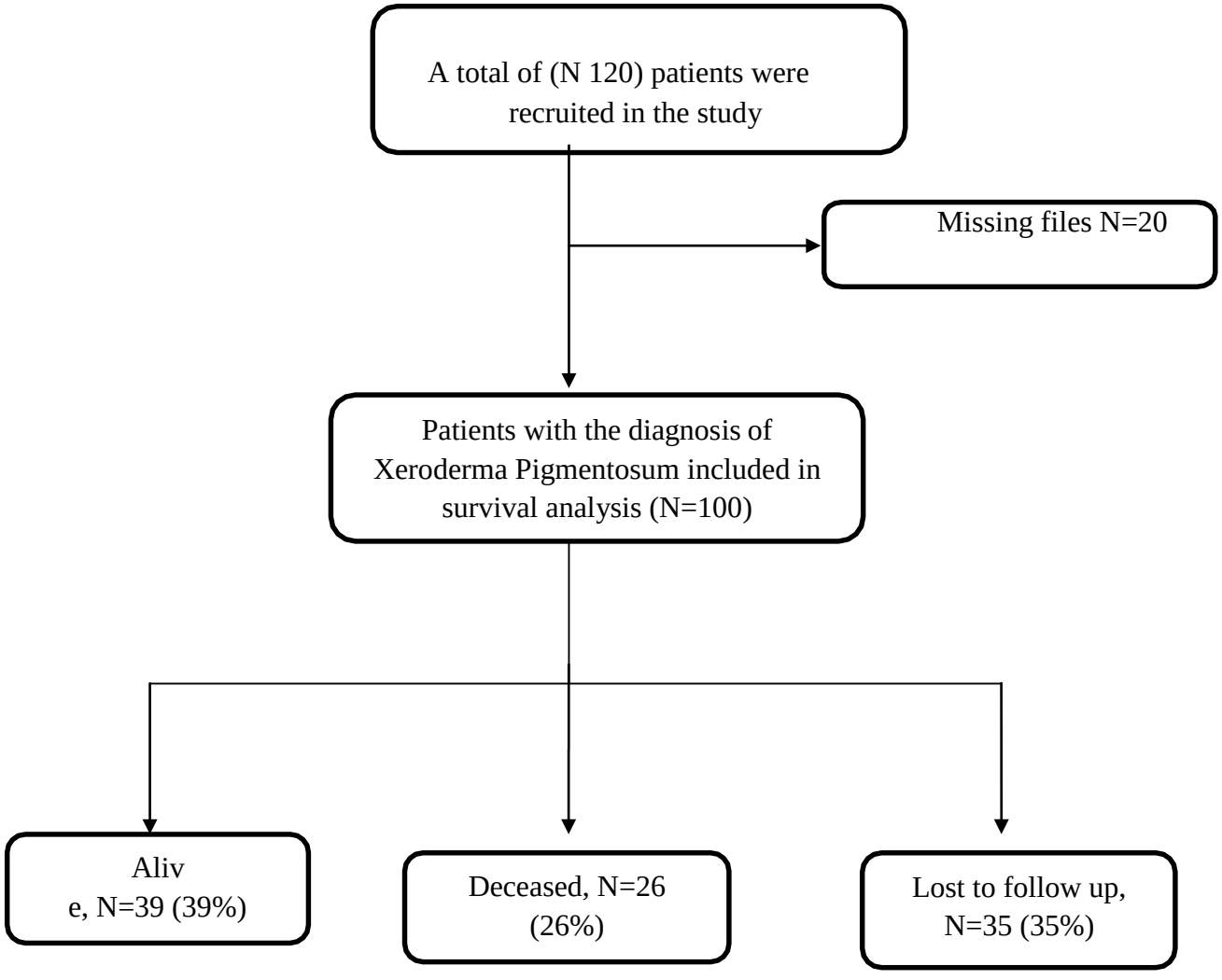


Figure 1 Flow chart showing enrolled study patients and their outcome

4.1 Baseline demographic characteristics of patients with Xeroderma Pigmentosum enrolled in our study

Medical records of 120 patients enrolled in the study were reviewed. Mean age at diagnosis was 5.4 years (SD ± 4.1) with a male to female ratio of 1:1 (M: F). Majority of the patient's parents had primary levels of education, 68% and 59% of fathers and mothers respectively. Eight patients had history of consanguinity and 36 patients had history of the disease in their families. Most of the patients, 69/96 (71%) originated from the coastal region of Tanzania. **(Table 1).**

Table 1: Socio-demographical profile of patients with Xeroderma Pigmentosum at MNH.

Variable	**Frequency (N=100)**	**Percent**
Gender		
Female	51	51
Male	49	49
Age Group, years (mean age =5.4 Sd ± 4.1)		
less than 5	64	64
5 to 9	20	20
10 to 14	13	13
15 to 20	3	3
Residence (n=96)		
Coastal regions	69	71.88
Non-Coastal regions	27	28.13
Father's Education		
No formal	4	4
Primary	30	30
Secondary	9	9
College/University	1	1
Not documented	56	56

Mother's Education		
No formal	12	12
Primary	26	26
Secondary	6	6
Not documented	56	56
History of consanguinity		
No	23	23
Yes	8	8
Not documented	69	69
Family History of XP		
No	40	40
Yes	36	36
Not documented	24	24

4.2 Clinical Characteristics of patients with Xeroderma Pigmentosum N=100 enrolled in the study

Majority of the patients (77%) developed their first symptom of XP before the age of 1 year. Cutaneous manifestation was found in almost all (99%) patients, while ocular findings were present in 93% patients. Oral findings were reported in 63% of patients, while only 5% of the patients had documented neural findings. Complete blood count on the first visit to the hospital was reported in 90% of patients, of which almost half of the patients (46%) had mild anemia and 7% had severe anemia **(Table 2)**

The most common cutaneous findings were hyper and hypopigmentation which were reported in 87% and 79% of the patients respectively. SCC of the skin was found in 41%, while other skin cancers including melanoma and BCC were rare, found only in 1% and 2% of patients respectively. Among the ocular findings, photophobia was the commonest, found in 84% of the patients followed by conjunctivitis found in 78% of patients and SCC involving the eye was found in quarter (25%) of the patients. Lip ulcer (57%), tongue lesions (38%) and oral SCC (15%) were the leading oral findings among the study patients **(Figure 2).**

Table 2: Clinical profile of patients with Xeroderma Pigmentosum enrolled in the Study

Variable	Frequency.	Percent
Skin changes		
Yes	99	99
Not documented	1	1
Neural changes		
No	10	10
Yes	5	5
Not documented	85	85
Oral changes		
No	2	2
Yes	63	63
Not documented	35	35
Eye changes		
No	1	1
Yes	93	93
Not documented	6	6
Age at first Presentation (years)		
< 1	77	77
1 to10	20	20
> 10	1	1
Not Documented Mean age 1.1±SD 1.8 years	2	2
HB Level g/dl		
< 7	7	7
7 to 9	19	19
> 9	64	64
Not Documented Mean Hb level 9.9±2.1	10	10

Hb: Hemoglobin; SD: standard deviation

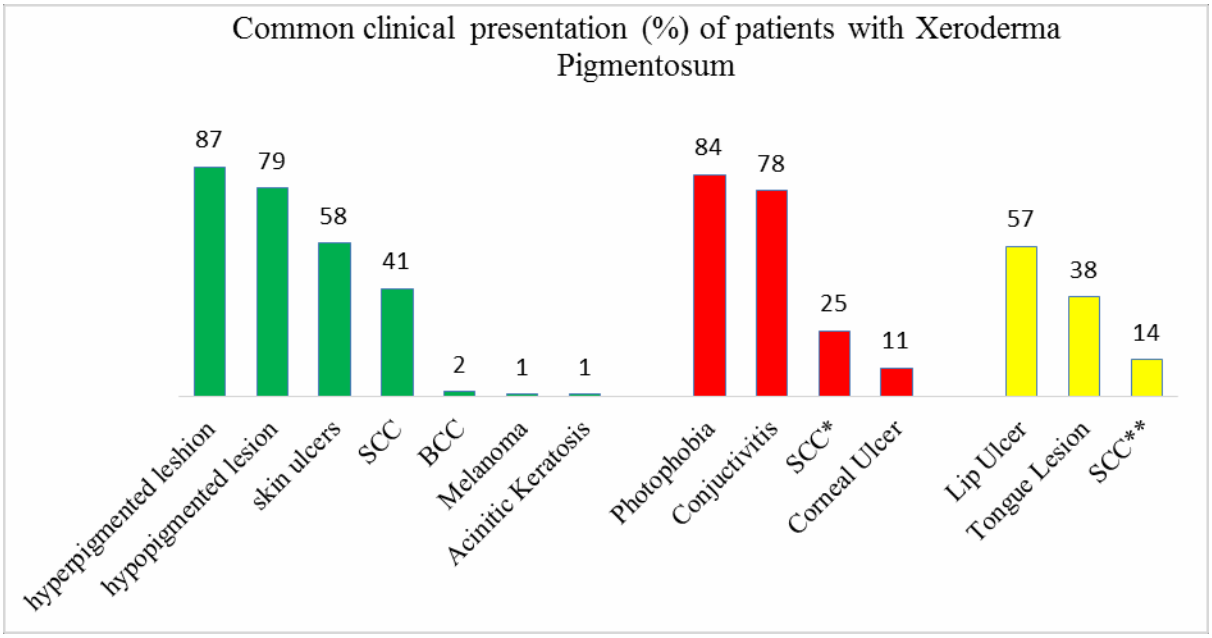


Figure 2: Bar graph showing common clinical presentation for patients with Xeroderma Pigmentosum enrolled in the study

*ocular squamous cell carcinoma **oral squamous cell carcinoma

Protective measure and treatment Modalities received by patients (N=100) with Xeroderma Pigmentosum enrolled in the study

Protective measures including hat, sun glasses and sun cream were received by 57%, 59% and 94% of patients respectively. With regard to treatment, Fluorouracil was received by 87% and retinoid was received by 85% of the patients. Those patients who had developed complications, 54% received surgical therapy, 31% received chemotherapy and 25% received radiotherapy **(Figure 3).**

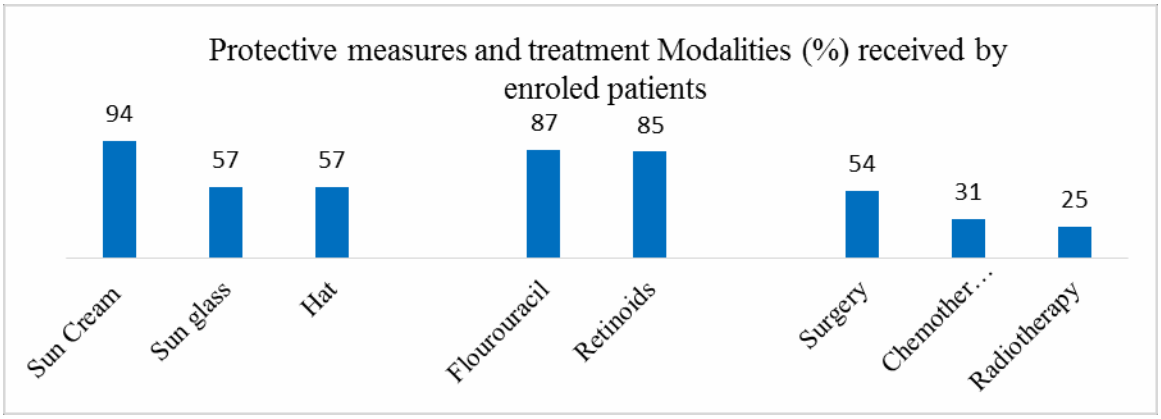


Figure 3: Bar graph showing protective measures and treatment modalities received by patients with Xeroderma Pigmentosum

Survival rates of 100 patients with Xeroderma Pigmentosum treated at MNH.

At the end of the study period (follow up period up to 9.5 years), 39% of enrolled patients were alive and still on active follow up, while 35% of patients had been lost to follow up and their status is not known. Death was confirmed in 26% of the study patients, and almost two third (65.4%) of the death were reported to occur at home.

The median survival time in years of patients diagnosed with XP in this study was 14.1 years (IQR= 11.7 – 17.2). Estimated overall survival rate (OS) was 90%, 64% and 46% at 5, 10 and 15 years respectively (Figure 4). Although results were not statistically significant, females had higher survival rates at 5 years compared to males (P=0.4), while males had higher survival rates at 10 years (Figure 5).

Xeroderma Pigmentosum patients who had developed cSCC had significantly lower survival rate compared to those who had no cSCC. The survival rate of XP patients with cSCC was 87% and 55% at 5 and 10 years respectively while it was 95% and 78% at 5 and 10 years respectively for non cSCC XP patients (p=0.02) (Figure 6).

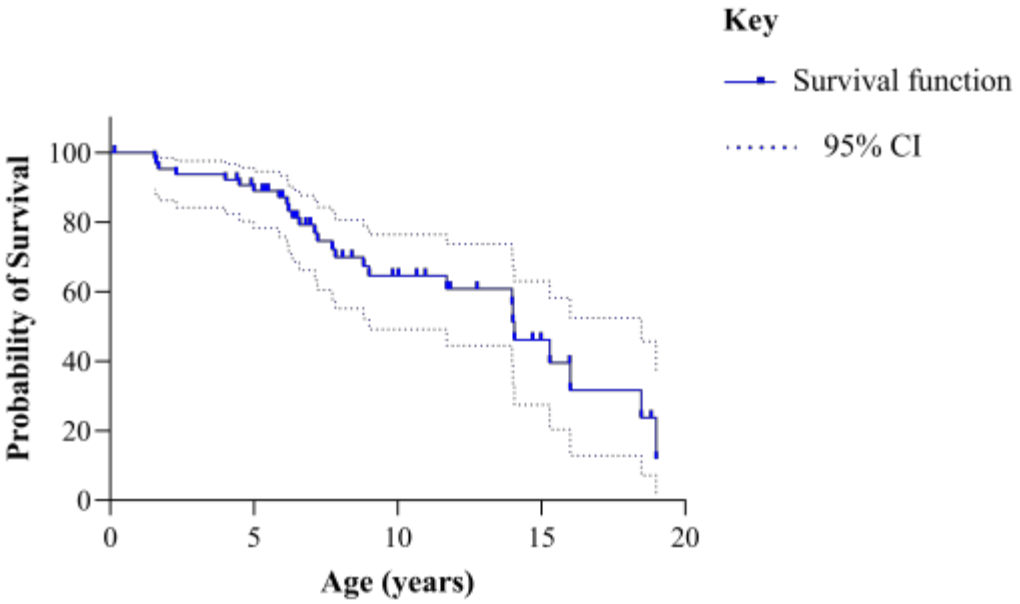


Figure 4: Kaplan –Meier Curves Showing Overall Survival

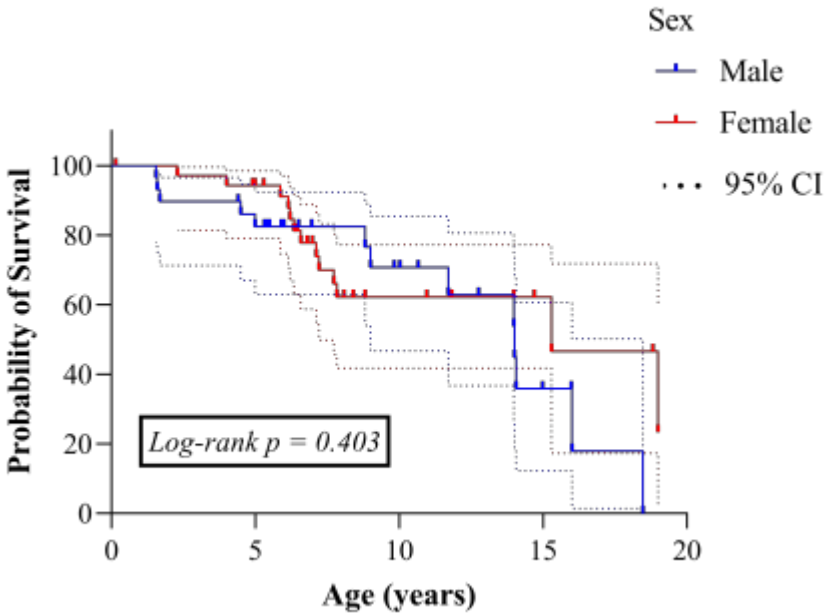


Figure 5: Kaplan –Meier Curves Showing Overall Survival by Sex

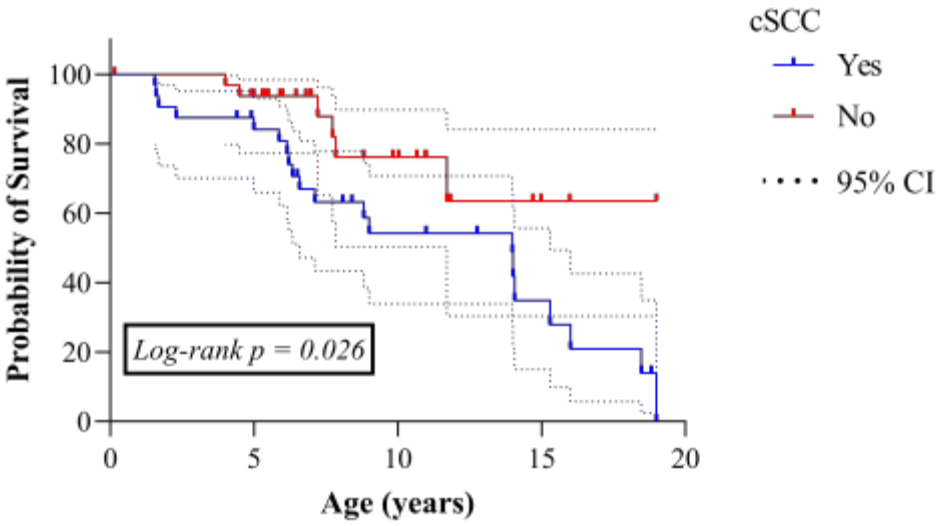


Figure 6: Kaplan –Meier Curves Showing Survival of patients by cSCC status

4.3 Factors associated with Mortality among patients with Xeroderma Pigmentosum enrolled in the study.

Of 100 patients in the study, 26 died, of which nine died in hospital and 17 died at home. Several factors have been reported to increase the risk of mortality in patients with XP. Findings from this study shows that, in univariate analysis, there was no significant difference in risk of death among patients with age greater than 5 years compared to patients with age less than 5 years (HR 12, 95% CI: 2.7-65.2 *P* =0.42). Patients with skin and ocular SCC had significantly higher risk of death, (HR 3.5, 95% CI 1.4-8.8, *P*=0.03) and (HR 2.45, 95% CI 0.96-5.51, *P* =0.03) respectively compared to those who did not have these types of SCC. Also, patients with photophobia had 11 times risk (HR 11.7, 95% CI 1.4-94.2, *P* =0.02) of death compared to those who did not have photophobia. With regard to treatment, those patients who had received radiotherapy (HR 2.35, 95% CI 1.0 – 5.2, *P* =0.03) were at increased risk of death compared to those who did not receive the treatments.

In a multivariate Cox regression analysis model adjusted for variables with $P \leq 0.2$ in univariate analysis, only cSCC was found to be significantly associated with increased risk of death. Patients with cSCC had twice as much (aHR 2.8, 95% CI 1.0-7.3, *P*= 0.02) risk of death than those with no cSCC **(Table 3).**

Table 3: Cox Proportional Hazards Analysis of Factors Associated with Death among patients with Xeroderma Pigmentosum

	Univar		Multivari	
Variable	**HR (95%CI)**	**P Value**	**aHR (95%CI)**	**P value**
Sex				
Female	1	1	1	1
Male	3.3(0.8-12.4)	0.07	0.9(0.3-2.9)	0.90
Age group (years)				
< 5	1	1		
5 and above	12 (2.7-65.2)	0.42		
History of consanguinity				
No	1	1		
Yes	1.3(0.5-3.8.4)	0.51		
XP history				
No	1	1		
Yes	1.4(0.5-3.6)	0.449		
Cscc				
No	1	1	1	1
Yes	3.5(1.4-8.8)	0.03	2.8(1.0-7.3)	**0.02**
Hypopigmented lesion				
No	1	1		
Yes	0.8(0.2-2.4)	0.73		
Hyperpigmented				
No	1	1		
Yes	1.5(0.3-6.7)	0.55		
Skin Ulcers				
No	1	1		
Yes	1.9(0.6-5.9)	0.21		
Conjunctivitis				
No	1	1	1	1
Yes	0.4(0.1-1.2)	0.11	1.3(0.4-4.1)	0.64
Corneal ulcers				
No	1	1		
Yes	1.1(0.3-3.9)	0.81		
photophobia				
No	1	1	1	1
Yes	11.7(1.4-94.2)	0.02	1.2(0.1-67.3)	0.83
SCC*				
No	1	1	1	1

Yes	2.4(1.0-5.5)	0.03	2.4(0.9-6.1)	0.
Lip ulcer				
No	1	1		
Yes	0.8(0.3-2.1)	0.77		
Tongue lesion				
No	1	1		
Yes	1.0(0.4-2.2)	0.98		
SCC**				
No	1	1		
Yes	0.4(0.2-1.8)	0.49		
Sunglasses				
No	1	1	1	1
Yes	2.1(0.8-5.3)	0.08	2.0(0.7-5.5)	0.
Hat				
No	1	1		
Yes	1.3(0.6-3.1)	0.43		
Suncream				
No	1	1		
Yes	1.5(0.3-6.7)	0.56		
Retinoids				
No	1	1		
Yes	0.6(0.2-1.6)	0.36		
Flourouracil				
No	1	1		
Yes	0.6(0.2-1.6)	0.62		
Chemotherapy				
No	1	1		
Yes	0.9(0.4-2.1)	0.93		
Radiotherapy				
No	1	1	1	1
Yes	2.3(1.0 – 5.2)	0.03	3.2(1.3 – 7.9)	0.
Surgery				
No	1	1		
Yes	1.2(0.5 – 2.8)	0.54		

*ocular squamous cell carcinoma **oral squamous cell carcinoma

Bold: Statistically significant at P value < 0.05

Abbreviation: CI: confidence interval , HR: Hazard Ratio, aHR , adjusted Hazard Ratio, cSCC- cutaneous squamous cell carcinoma

5.0 DISCUSSION

A total of 100 medical records of patients with XP treated at the Pediatric oncology unit and Dermatology clinic at MNH from June 2011 to December 2020 were retrospectively reviewed. The aim was to understand the epidemiological profile, clinical profiles, treatment modalities and survival outcomes for patients treated with XP at our facility.

Observed male to female ratio in this study was 1:1. Similar findings were reported in previous studies (1,10,16). This is in line with the mendelian law of inheritance whereby male and female are equally affected in an AR disease. Xeroderma Pigmentosum is a hereditary condition which runs through the family and passed from one generation to another. Two copies of an abnormal gene must be present to develop the disease. In this study Family history of XP was seen in 36% consistent with previous report by Bhutto AM *et al* (12). The 26% rate of parental consanguinity observed in this study was lower compared to those reported in Turkey and Libya but higher than that reported in South Africa (5,16,33). Cultural difference has contributed significantly to the findings where by consanguineous marriage is practiced more in Asia and Northern Africa compared to sub-Saharan countries (34). In Tanzania, consanguineous marriage is more prevalent in coastal regions where most of the patients from this study originated, an area affected by Asian culture due to historical trade in 20th century.

Symptoms of XP start to develop following repeated sunlight exposure (1), the average age at the onset of signs of XP in our patients was 1.15 years (13.8 months), age at which toddlers are frequently exposed to sunlight as they have attained walking milestone enabling them to walk and play outside. Also, parents feel comfortable taking their infants out around this age group. Similar findings were reported in Turkey, Libya and Europe. Normally symptoms are limited to sun exposed areas with skin at large, anterior part of the oral and ocular structures. The distribution of symptoms/signs of patients in this study followed the natural cause of the disease with skin being the most common affected organ followed closely by ocular involvement, findings in line with previous studies. (1,5,9,12,16,17). Neural changes were the least observed presentation. Study done in Pakistan, Libya and S. Africa reported no patient had neurologic abnormalities in their study while up to 30% of the patients had neurological involvement in studies done in

USA, Europe and Japan (4–6,12,33,35). These findings were not observed in this study partly probably due to the fact that not all patients had their central nervous system examination well documented. And partly due to differences in genetic subgroup among different ethnicity. Xeroderma Pigmentosum subgroup A (XPA), subgroup D (XPD) and subgroup G (XPG) which are commonly present with neurological abnormalities are found frequently in Japan, USA and Europe. Also, neurologic abnormalities occur later in life and almost 90 percent of patients in this study were below 9, this could have led to miss those patients who will develops neurological signs (36).

Since at present there is no definitive cure for XP and gene therapy as the cure for XP is still in the development, protection from the sunlight remain essential for halting the progression of the disease (8,18). Patients in this study were routinely receiving hats, sun cream, sun glasses, fluorouracil and retinoids subjected to availability, though most of the patients had already developed complications at their first visit that were meant to be protected by using these measure hence decreasing its efficacy. Also, poor compliance to these measure among patients also reduce their effectiveness in protecting disease specific complications.

Studies have shown that XP patients have lower survival rate than general population (6). Observations from this study shows that the median survival time of 14.10 years and the overall 5-year survival rate of 90% was relatively lower than 32 years and survival rate of 99% that was reported by Bradford T, in USA (6). The difference in survival time and survival rate between these two groups could be attributed to many factors including difference in sun UV light exposure, quality of care received by patients in these different settings influenced by early diagnosis, availability of advanced treatment, follow up, nutrition and others. Rarely people of skin color (POC) develops skin cancer in the absence

of risk factor, the low incidence of skin cancers in darker skinned groups is primarily a result of photo-protection provided by increased epidermal melanin, which filters twice as much UV radiation as does that in the epidermis of Caucasian (27,28). In the presence of risk factor like XP, skin cancer in POC often present with an advanced stage, and thus, worse prognosis in comparison to Caucasian patients. This could be another factor behind the relative low survival of patients this study (27).

Xeroderma Pigmentosum patients have 10000-fold risk of developing cSCC compared to general population which could lead to various complications that eventually lead to death (1). In this study, those who developed cSCC were observed to have low survival rate compared to those who did not, similar to previous report of the study done in USA(6). The overall 5-year survival rate of patients with cSCC in this study was 87%, similar to that reported in USA (90%) and Europe (19,22). Other studies which reported very low survival rate, their patients had advanced stage of cancer with various comorbidities which was not assessed by this study and may thus limit the comparability (21,25).

Cutaneous squamous cell carcinoma is associated with cumulative, prolonged UV-exposure, which causes substantial systemic immune suppression, as well as chronic diseases associated with a weakened immune system or immunosuppressive (29,30). It carries a low but significant risk of metastasis and death (31). Size, location and stage of the tumor associate with the mortality rate (31). In this study, cSCC was a strong predictor of mortality in patients with XP. Survival rate for XP patients who developed cSCC was lower compared to those who did not develop cSCC. This is in line with the previous reports by Bradford T *et al* and Condict M *et al* (6,32). Effort should be made to diagnose patient with XP at the earliest and immediate rigorous protection from UV light should be initiated to prevent these patients form developing cSCC which carries unfavorable outcome.

5.1 Strength of the study

To the best of my knowledge, this is the first study directly looking at clinical profile, treatment and outcome of children with xeroderma pigmentosum in Tanzania. with XP in Tanzania. Phone call follow up of patients treated at the units allowed identification of patients who were still alive or died at home, hence reduced the number of loss to follow up.

5.2 Study Limitation

Missing of data or/and information was a major limitation of this study which might have led to bias. (example; exact date of first symptoms presentation, exact time an event such as death occurred, during the phone call interview etc.)

6.0 CONCLUSION AND RECOMMENDATION

6.1 Conclusion

Xeroderma Pigmentosum is an inherited disease which affects male and female equally. Skin and eyes are the most affected organs and can be protected by using protective measures such as sun cream and hats. Survival of the patients with XP is progressively decreasing from 90%, 64% and 46% at 5, 10 and 15 years respectively. Those XP patients with cSCC had lower survival rate compared to those with no cSCC which was found to an only predictor of mortality in patients with XP.

6.2 Recommendation

Cutaneous squamous cell carcinoma poses a significant impact on the survival outcome of patients with Xeroderma pigmentosum. We recommend early identification of patients with XP and initiation of preventive measures to reduce morbidity and mortality. This can be achieved by raising awareness among health care workers and the community, and by educating parents of patients with XP regarding the prevention of cSCC.

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APPENDICES

Appendix 1: Data Extraction Tool

Study title:

Checklist Number: ☐

Date:____/_____/_____

Parent or Guardian Cell phone ☐ Number:

SECTION A: BIODATA AND SOCIODEMOGRAMPHICS OF THE PATIENT

Qn1 Patient identification Number …….

Qn2 Date of admission /visit to the Hospital

Qn3 Date of birth ……

Qn4 Gender (tick)

0= Male

1= Female

Qn5 Tribe specify ……

Qn6 Father's education level

0 = No formal

1= Primary

2 = Secondary

3 = College/University

Qn7 Mother's education level

0 = No formal

1= Primary

2 = Secondary

3 = College/University

Qn8 History of Consanguinity

0= No

1 = Yes

2 = Not Documented

Qn9 If Yes in Qn8

1=First cousins

2= Second cousins

3 = Others

4= Not documented

Qn10. Family History of XP

0= No

1 = Yes

2 = Not Documented

Qn11. If yes in Qn10,

1=Parents

2=Siblings

3= Grand parents

4=Others

5= Not documented

SECTION B: CLINICAL PROFILE

Qn12. Age of child at 1st presentation

Q12a. Age in years …….

Q12b. Age in months …….

Qn13 Symptoms duration prior to 1st visit/ admission

Q13a. Duration in years …….

Q13b. Duration in months …….

Q13c. Duration in weeks …….

SIGNS AND SYMPTOMS AT PRESENTATION

Qn14 Skin Changes

1=Yes

0=No

2= Not documented

Qn15 If yes in Q14a

1=Sun burning

2= Hyperpigmented lesions

3= Hypopigmented lesions

4= Ulcers

5= Actinic keratosis

6= keratoacanthomas

7 = Malignancy, specify

Qn16 Eyes changes

1=Yes

0=No

2= Not documented

Qn17 If yes in Qn16

1=Photophobia

2= Conjunctivitis

3= Corneal keratitis

4= Malignancy, specify

5= Others, specify

Qn18 Oral changes

1=Yes

0=No

2= Not documented

Qn19 If yes in Qn18

1=Lip ulcer

2= tongue lesions

3=Malignancy, specify

4=Others, specify

Qn20 Neural changes

1=Yes

0=No

2= Not documented

Qn21 If yes in Qn20

1= hearing loss

2= mental retardation

3= abnormal speech

4= Others, specify

RADIOLOGY RESULTS (MRI/CT)

Qn22 Was MRI/CTdone?

1=Yes

0=No

2= Not documented

Qn 23 If yes in question 22 above, what are the findings

1. Cortical atrophy
2. Ventricular dilatation
3. Glioma
4. Others

Qn 24 Was Full blood picture done?

1=Yes

2=No

3=Not documented

Qn25 If yes in question 24 above

1. Haemoglobin level ……..
2. Platelets count …….

SECTION C: TREATMENT MODALITIES

Qn26 Date of diagnosis ……

Qn27 Date of treatment initiation……..

Qn28 Preventive Measures

1=Yes

0=No

2= Not documented

Qn29 If yes in Qn26

1=Hat

2= Sun glasses

3= sun cream

4= not documented

Qn30 Treatment of complications

1=Yes

0=No

2= Not documented

Qn31 Pre- malignancy treatment if Qn28 is yes

1. Retinoids
2. topical 5-fluorouracil
3. imiquimod
4. others, specify

Qn32 Malignancy treatment if Qn28 is yes

1. Chemotherapy
2. Radiotherapy

Surgery

SECTION D: OUTCOMES

Qn33 What is the status?

1. Alive
2. Dead
3. Lost to follow up

Qn34 Are the disease symptoms improving, worsening or the same? If alive

1. Improving
2. Worsening
3. Same

Qn35 What is the duration of time from diagnosis to death? If dead

1. Days …….
2. Weeks……
3. Months…….
4. Years ……

Appendix 2: Structured Mobile Interview (English version)

Study ID: ……..

Date of the interview: …….

Mobile number: ……..

Name of the interviewer: …….

E1	Relationship with the child	1. Father 2. Mother 3. Other,
E2	How is the child doing since discharge / last visit from the hospital?	1. Improving 2. Worsening 3. Same 4. Passed away
If the child passed away (G4) pause and console her/him, ask if she/he is comfortable to continue with the discussion or postpone		
E3	If the child passed away, do you remember when?	1. Yes (date_____) 2. No
E4	Where did the child pass away?	1. Home 2. Hospital 3. On the way to the hospital 4. Others specify

Appendix 3: Mahojiano kwa Njia ya Simu (Swahili version)

Namba ya utambulisho …….

Tarehe ya mahojiano: ……

Namba ya simu ……..

Jina la mhojaji: ……..

Jina la mhojiwa……....

E1	Uhusiano na mtoto	1. Baba 2. Mama 3. Ingineyo
E2	Maendeleo yam tot yapoje toka kuruhusiwa hospitali?	1. Hali ni nzuri 2. Hali si nzuri 3. Alifariki
Endapo mtoto alifariki (G4) sitisha mahojiano kwa muda na mpe pole kwa kufiwa. Kisha uliza endapo anaweza kuendelea kushiriki mahojiano ama kuahirisha mazungumzo.		
E3	Endapo mtoto alifariki, unakumbuka alifariki lini?	1. Ndiyo, Tarehe…….. 2. Hapana
E4	Mtoto alifariki wapi?	1. Nyumbani 2. Hospitali 3. Njiani kuelekea hospitali 4. Kwingineko, orodhesha

Appendix 4: Verbal informed consent form (English)

Study ID: _____

MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES (MUHAS)
A VERBAL CONSENT FORM FOR STUDY ON CLINICAL PROFILE, TREATMENT AND OUTCOME OF CHILDREN WITH XERODERMA PIGMENTOSUM AT MUHIMBILI NATIONAL HOSPITAL, DAR ES SALAAM, TANZANIA.

Introduction

My name is Dr Hajaj Mohamed Salum, a resident at Muhimbili University of Health and Allied Sciences, Dar es Salaam. I'm doing a research on clinical profile, treatment and outcome of children with xeroderma pigmentosum at Muhimbili National Hospital, Dar es salaam, Tanzania. I am going to give you information and invite you to be part of this research. Before you decide, you can talk to anyone you feel comfortable with about the research.

Purpose of the research

The purpose of this research is to determine clinical profile, treatment and outcome of children with xeroderma pigmentosum, as it will help in prioritizing care on patients based on their risk factors so as to improve their survival and quality of life in general.

What does participation involve?

This research will involve answering few questions regarding the well-being of your child and it will take about 5 minutes via a mobile interview. Your participation in this research is entirely voluntary.

Confidentiality

Information that will be collected during the research will be kept confidential and no-one but the researchers will be able to see it, no names will be used but identification numbers only. We will not be sharing the identity of those participating in the research.

Risks

By participating in this research, you will not be subject to any risk.

Benefits

You may not likely have any direct benefit from being in this study, but the results will be used for improving the care of other patients.

Consent section:

Do you wish to participate?

A. Yes……...

B. No ……...

Name: ……...

Name of the person obtaining a consent: ……... Date: ……

Appendix 5: Fomu ya Maneno Ridhaa (Swahili Version)

Namba ya utambulisho: _____

KICHWA CHA HABARI: UTAFITI KUHUSU WASIFU WA KLINIKI, MATIBABU NA MATOKEO YA WAGONJWA WENYE XERODERMA PIGMENTOSUM WANAOHUDHURIA HOSPITAL YA TAIFA YA MUHIMBILI, DAR ES SALAAM, TANZANIA.

Utangulizi:

Habari, naitwa Daktari Hajaj Mohamed Salum mwanafunzi washahada ya uzamili ya udaktari wa watoto katika Chuo cha Sayansi Shirikishi cha Muhimbili. Nafanya utafiti kuangalia utafiti kuhusu wasifu wa kliniki, matibabu na matokeo ya wagonjwa wenye xeroderma pigmentosum wanaohudhuria hospital ya taifa ya muhimbili, dar es salaam, tanzania, na ningependa kukukaribisha kushiriki katika utafiti huu. Nitakupa maelekezo na kukualika kushiriki katika utafiti huu.

Lengo la utafiti huu: lengo ni kuchunguza hali ya kiafya ya watoto wa Xeroderma Pigmentosum baada ya matibabu katika hospitali ya taifa ya Muhimbili. Hii itasaidia katika kutanguliza huduma kwa wagonjwa kulingana na sababu zao za hatari ili kuboresha maisha yao na ubora wa maisha kwa ujumla

Kushiriki kutahusisha nini:

Kama unakubali kushiriki katika utafiti huu, utajibu maswali maswali machache kuhusu hali ya mtoto, na itachukua takibrani dakika 5 kupitia njia ya simu. Kushiriki kwako ni kwa hiari

Usiri wa taarifa: taarifa zote zitakazopatikana katika utafiti huu, zitabaki kuwa siri, tutatumia namba ya hospitali na namba ya utambulisho ya utafiti huu kwa ajili ya kuwatambua washiriki wa utafiti bila kutumia majina katika utafiti huu au katika machapisho yoyote ya kiutafiti yatakayotokana na utafiti huu hapo baadae

Madhara ya kushiriki

Kwa kushiriki kwenye utafiti huu hautapata madhara yeyote.

Faida za ushiriki

Unaweza usifaidike kwa moja kwa moja kutoka kwenye utafiti huu, ila matokeo ya huu utafiti yatatumika kuboresha huduma za watoto wetu.

Tamko la ridhaa:

A. Ndiyo ……

B. Hapana …….

Jina la mtoa ridhaa: …….

Jina la mwomba ridhaa…… Tarehe ……