International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 4 July-Aug 2022, pp: 393-397 www.ijprajournal.com ISSN: 2456-4494

Review On: Xeroderma Pigmentousum

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Submitted: 01-07-2022 Accepted: 14-07-2022

ABSTRACT:
Xerodermapigmentosum (XP) is a rare disorder of defective UV-radiation induced damage repair that is characterized by photosensitivity with easy skin burning following minimal sun exposure, early freckling and development of lentiginous pigmentation along with other features of poikiloderma and a propensity for developing skin cancer at an early age. Xeroderma pigmentosum (XP) is a rare autosomal genodermatotic that manifests clinically with pronounced sensitivity to ultraviolet (UV) radiation and the high probability of the occurrence of different skin cancer types in XP patients. XP is mainly caused by mutations in XP-genes that are involved in the nucleotide excision repair (NER) pathway that functions in the removal of bulky DNA adducts. Besides, the aggregation of DNA lesions is a life-threatening event that might be a key for developing various mutations facilitating cancer appearance. One of the key players of NER is XPC that senses helical distortions found in damaged DNA.

KEYWORDS:Lentiginous, Minimal, Poikiloderma,Genodermatotic, Manifests

I. INTRODUCTION[1-2]:

Dermatologist Moriz Kaposi first described xeroderma pigmentosum in 1874. Dr. Kaposi described patients with dry skin, pigmentary changes, and the development of multiple skin tumours at a young age. Further studies over the next several decades highlighted the importance of severe photosensitivity in the pathophysiology of xeroderma pigmentosum. In the 1960s, Dr. James Cleaver performed studies on cultured fibroblasts from patients with xeroderma pigmentosum and found the fibroblasts to have defective DNA repair after UV exposure. Further studies showed that patients with xeroderma pigmentosum with neurologic manifestations have even less effective DNA repair after UV exposure compared to patients with XP without neurologic manifestations. These studies have enhanced knowledge about the connections between UV exposure, DNA damage and repair, and the development of malignant tumours. XP is a rare disorder transmitted in an autosomal recessive fashion characterized by photosensitivity, pigmentary changes, premature skin ageing and neoplasm development (Cleaver, 1968). While XP may be rare the nature of the intrinsic defect in the affected individuals is of great interest especially when it occurs in siblings. In this series we present five cases of XP, four familial and one sporadic.It is an inherited condition charoctinged by an extreme sensitivity to UY Rays from sunlight. Areagenerally which get affected [3]

A) Eyes
B) Ears
C) Skin

➢ Note: -Some affected individuals also have. Problemwith Nervous system.

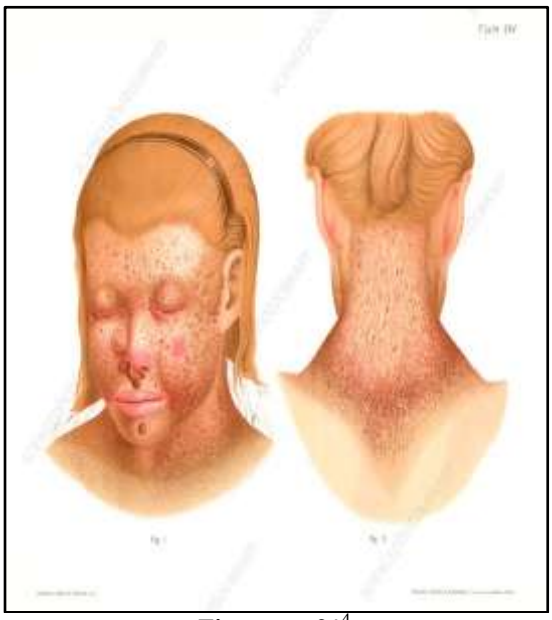

Figure no.01[4]

ETIOLOGY OF THE DISEASE[5]:

Xeroderma pigmentosum results from a mutation in nucleotide excision repair. The nucleotide excision repair system is capable of removing ultraviolet-induced damage to DNA,

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such as pyrimidine dimers and pyrimidines 6-4 pyrimidones. The progression of xeroderma pigmentosum is due to the accumulation of unrepaired DNA damage. Eight different mutations have been found to associate with different subtypes and clinical presentations of xeroderma pigmentosum. Research has described the subtypes of XP A-G and XP variants, each with varying mutations in nucleotide excision repair. A mutation in the gene XPC results in the most common subtype in the United States

XPC gene codes for an endonuclease and is on chromosome 3p25. The mutated endonuclease is unable to sense damage in DNA, resulting in severe sun sensitivity and malignant tumour formation of the skin and mucous membranes. The XPC subtype of xeroderma pigmentosum has no neurologic manifestations compared to the XPA subtype, which is the most common form in Japan.

The XPA gene codes for DNA damage binding protein 1 (DDB1) is on chromosome 9q22. DDB1 normally senses damage in DNA and assists in the unwinding of DNA. These patients present with both skin and neurologic manifestations of the disease.

SIGNS AND SYMPTOMS[6]

- Generally, signs of XP usually appear in infancy or early childhood.
- Affected children developed a severe sunburn after just spending few minutes in the sun.
- Sunburn causes (TO affected patient) heavy Rednessof skinand blistering of skin.
- It is maximum seen at the age of 2 in many of the cases.

SOME COMMON SIGNS DUE TO XERODERMA PIGMENTOSUM[7]: -

1) Freckling: -

- After affecting By XP "developed Freckling of sun exposed are observed (such as on Fare, arms and lips)
- people with XP have generally increased the Risk OF developing skin.

2)Cancer: -

- Without any skin protection. about half of children with this condition developed their Skin cancer by age of 10 itself
- This type of skin. often seen on cancer areas like generally Face, Tips and eyelids
- Cancer Can developed on scalp, in the eyes and on the tip of tongue.
- Studies suggested that people also have increased risk of other cancer, including Brain tumour

3) Blood shot and irritation:

The eyes people with XP may Be Sensitive to UY Rays OF fromSun, that is if eyes are notprotected from Sun, they may lead to Blood Shot and irritation and clear Front convering of eyes and may Become cloudy.

4) Eye Lashes:

In some people eyelashes fall out and the eyelids may be thin and turns abnormally inwards or outward and in the addition to increased risk of eye cancer, xeroderma pigmentosum is associated with non-cancerous growth on eye.

5) Neurological abnormalities:

About 30% of people with xeroderma pigmentosum developed progressive neurological abnormalities to problems involving skin and eyes.These abnormalities may include hearing loss (dumbness),poor concentration, movement problems , loss of intellectual functions, difficulty in swallowing and ranking and selizure.

SOME OF THE COMMON SYMPTOMS DUE TO XERODERMA PIGMENTOSUM

1) xerosis or dry skin
2) Increases skin pigmentation
3) Skin atrophy or skin thinning
4) Telangiectasis, i.e., the widening of small blood vessel resulting in thread like pattern on skin.

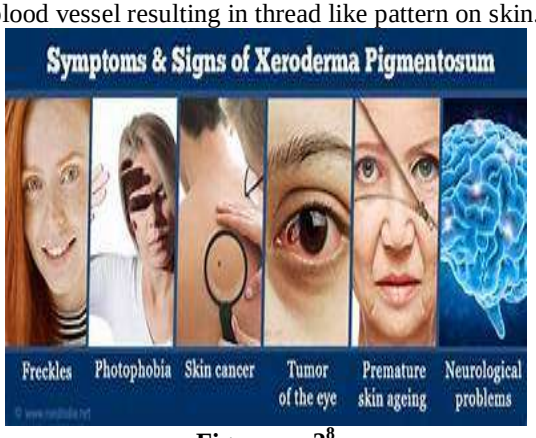

Figure no.2[8]

relation of xeroderma pigmentosum with cancer[7]: -

- People with XP also have on increased chance of developing of skin cancer.
- The Risk of developing non-melanoma skin cancer, such as Basal cell,

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Carcinoma or squamous cell carcinomais 1000 timeshigher among people

With xerodermapigmentosum,compared with the general population.

- Squamous cell carcinoma may form on the tip of the tongue. for example, the risk of developingmelanomais 200 times greater.
- Among the people who devolved melanoma this typically happen at about the age 22 itself.

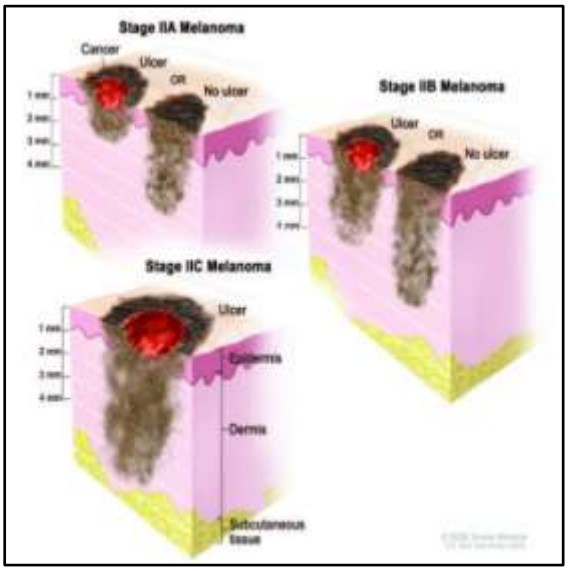

Figure no.03

Diagnosis For Xeroderma Pigmentosum[9]:

- XP is suspected when a person shows signs of extreme Sun sensitivity.
- Signsof sun sensitivity include severe Burning and Blistering with only a small amount of sun exposure or ever exposure to indoor Florent light
- The Genetic testing for mutation in gene associated with xeroderma pigmentosum available mainly as a part of research Studies Because there are at least 8genes associated with xeroderma pigmentosum,laboratoryscreening test are recommended to help to determine which of the 8 gene is likely to Be causingxeroderma in a family.
- Approximately one person per million suffer From Xeroderma pigmentosum except For in a Few locationsthat shows Founder effect. The rarity of the diseases means that diagnosis is not frequently required, hence Robust Diagnostic method not been developed.
- Many who have engaged in basic research into the genetic and molecular basis of xeroderma pigmentosum has provided informal services for patients and parenteral diagnosis using specialized DNA repair tequnices.

Medication For Xeroderma Pigmentosum [10]:

- Oral retinoids have been decreased the incidence of skin cancer in patient with xeroderma pigmentosum
- This therapy is limited by done related irreversible calcification of ligaments and tendons.
- Chemical therapy with 5-Flurouracil may be useful actinic keratoses.

EXAMPLES OF MEDICATIONS:

1) **Oral retinoids:** Isoteritinol drug
2) **Antineoplastic agents:** 5-Fluro uracil

OTHER TREATMENTS MAY INCLUDE:

1) Chemotherapy
2) Anti-cancer drug (Malignancy)
3) Anti-histamines which can reduce the inflammations.

Medical Care For Xeroderma Pigmentosum:

The goal the treatment is to protect the patient from sun light. To this end, regular visit to the dermatologist might be very necessary for the purpose of patient education and early detection of the diseases and the treatment for any types of malignancies.

Figure no: - 04[11]

The use of sun cream in the conjugation with the other sun avoidance methodology protective clothing and eye wears can minimize UV induced

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damage in the patient with Xeroderma pigmentosum.

Causes Of Xeroderma Pigmentosum[12]:

1) Xeroderma Pigmentosum caused by mutation in gene that are involved in repairingDamage DNA.
2) DNA also can be damaged by UV rays too from sun and from toxic chemicals such as those found in Cigarette smoke.
3) Many of the gene released to xeroderma pigmentosum are the part of DNA repair process known as Nucleotide Excision Repair (NER)
4) The major feature of xeroderma pigmentosum result from build-up of unpaired DNA damage.
5) When the UV rays Damage Gene that control cell growth and cell can Die or Grow Faster.
6) Those with condition like skin blistering are particularly prone to skin cancer, as well as often to developing eye and neurological problems, can be the causes of xeroderma pigmentosum

Inheritance Of Xeroderma Pigmentosum[13-14]:

This condition is the inheritance an autosomal recessive pattern, which means both the copies of the gene in each cell have mutation. The parents of the individuals with an autosomal recessive condition each carry one copy of mutated gene but they topically do not shows sign and symptoms of conditions.

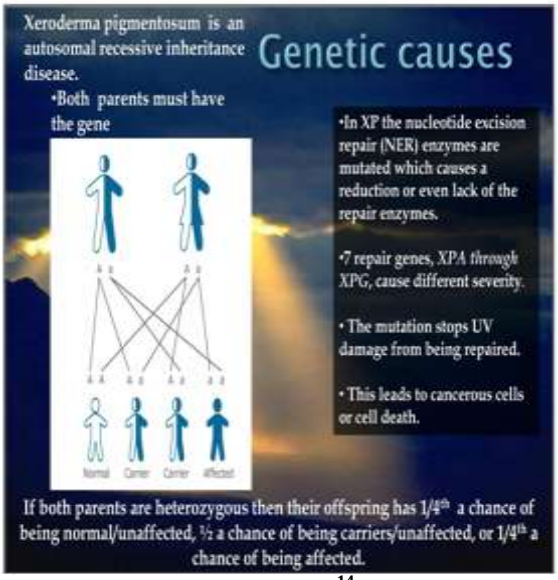


Figure no 05[14]

GLOBAL NUMBER OF PATIENTS OF XERODERMA CURRENTLY[15]:

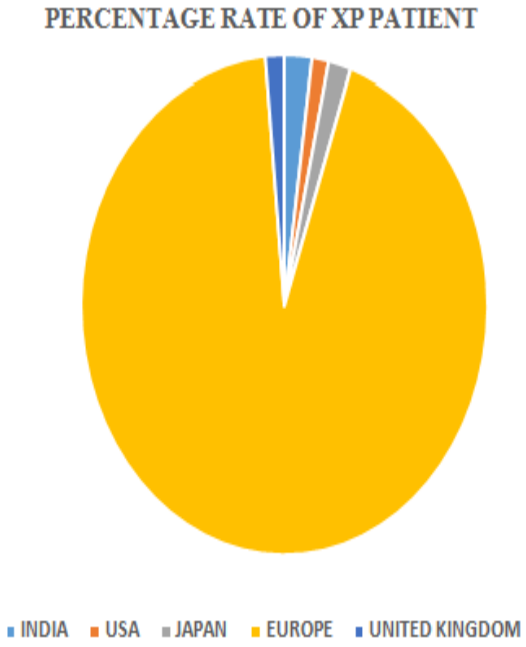
- Comparatively the rate of xeroderma pigmentosum patient is very less, as explained below in the example: -

1) One patient is found among 1 lakh peoples worldwide.
2) One patient is found among 370 peoples in India
3) One patient id found among 25,000 peoples in USA
4) One patient id found among 22,000 People in Japan
5) One patient is found among 4,30,000 in Europe
6) One patient among 1,000,000 In whole United Kingdom.

- **IN INDIA: -**

Xeroderma pigmentosum is very rare autosomal diseases recessive disorder associated with defective DNA repair which causes Photosensitivity.

And as we known that Photosensitivity leads to pigmentary chargers autrophy and later squamous cell carcinoma.



SOME LATEST REPORTS ON XERODERMA PIGMENTOSUM[16-17]:-

- So far 29 cases are reported from India of xeroderma pigmentosum

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- Xeroderma id rare autosomal Geno dermatosis with worldwide incidence of 1: 250,000 live births.

CHEMOPREVENTIONS OF SKIN CANCER IN XERODERMA PIGMENTOSUM[18] :

- Dr John di Giovanna Gary perk of dermatology Branch, NCI Robert. Tarone of NCI Alar Mashell ofnational is institute of Arthritis, muscle skeletal and skin diseases.
- Dr Kraemer embarked or a study NY to attempt to prevent new SKID cancer in XP patient using A denvatives Those agents asso & cued with promotion of normal differentiation.
- They selected 5 xeroderma patient with high Frequency of new primary skin cancer,cataloguedare removed all of their cancer surgically for a period of 2 years and with high oral 13-cis retinoic acid.

II. CONCULSION[19]:

Although there is no cure for xeroderma pigmentosum, increased awareness and crucially early diagnosis followed by the rigorous protection from day light and carefully patient management can be dramatically improved the quality of the life and life expender of affected individuals

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