Original Article

Assessment of "Imtiaz's Sign" for Early Detection of Hypovitaminosis A

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Purpose: To identify and document the earliest diagnostic sign of vitamin A deficiency (Imtiaz's sign).

Material and Methods: This prospective case series study was conducted from September 1999 to September 2014 at ophthalmology department Chandka medical college and Syed eye clinic, Larkana, Pakistan. Patients identified clinically as cases of hypovitaminosis A on the basis of presence of "Imtiaz's sign" were included in the study. Patients with Retinitis pigmentosa, glaucoma, chronic liver disease and malabsorption syndrome were excluded from the study. Imtiaz's sign of vitamin A deficiency and nyctalopia were noted and relevant laboratory investigations available were also done on selected patients. Patients were given therapeutic doses of vitamin A and improvement was observed to see resolution of Imtiaz's sign of vitamin A deficiency and remission of nyctalopia.

Results: 650 patients, 152 (23.38%) males and 498 (76.62%) females were identified as cases of hypovitaminosis A on the basis of presence of Imtiaz's sign. Age of the patients ranged from 5 to 43 years and the mean age (± standard deviation) was 18.15 ± 10.20 years. All patients replied positively for nyctalopia; however other signs, except Imtiaz's sign, were not observed due to the early stage of vitamin A deficiency. Relevant laboratory investigations were performed on selected cases which showed that 45.68% of them had iron deficiency, 40.74% of them had hypoalbuminemia and 13.58% had disturbed LFTs. This shows that most of the patients suffering from vitamin A deficiency were victims of malnourishment.

Conclusion: Imtiaz's sign is an early and effective clinical diagnostic sign to identify vitamin A deficiency at an early phase. It requires no costly tools for application, is safe and can be easily recognized and treated by vitamin A supplements. Such a diagnostic ocular sign is desirable to avoid morbidity and mortality related to vitamin A deficiency.

Keywords: Blindness, Malnutrition, Vitamin A deficiency, Xerophthalmia.

Vitamin A, a fat soluble vitamin, was the first vitamin to be discovered in 1913.[1] Chemically it is a Retinol, and is the immediate precursor of two very important metabolites, Retinal and Retinoic acid. Retinal is a very important component of rhodopsin which is mandatory for functioning of photoreceptors and Retinoic acid has a vital role to play as messenger during transcription of a number of genes. Vitamin A is essential to human body as it is an important part of visual purple of both rods and cones and serves both night and day vision. As the rods are affected first in hypovitaminosis A, night blindness has become a famous feature of vitamin A deficiency. Vitamin A also maintains epithelia of skin and mucous membranes all over the body and is also needed for spermatogenesis, female reproductive cycle and

skeletal development and maintenance. Its immune strengthening function has led to the popularity of this vitamin as anti-infective.[2] Approximately one third of the world's preschool-age population is estimated to be suffering from Hypovitaminosis A; with the highest prevalence (44-50%) being reported from South – East Asia and Africa.[3] One of the earliest studies carried out in Indonesia showed that children with night blindness were almost three times more likely to die as compared to those from the same community without night blindness, and children with both night blindness and Bitot's spots were almost nine times more likely to die.[4] A study from Bangladesh showed that almost two-thirds of children with Keratomalacia had died within a few months[5]. These facts clearly indicate that irreversible damage has been done by the time the ocular signs develop. The different ocular signs and symptoms of vitamin A deficiency, as graded by the WHO[7], are:

- Night blindness.
- Conjunctival xerosis.
- Bitot's spots.
- Corneal xerosis.
- Corneal ulcer covering less than $^1/_3$ of the cornea.
- Corneal ulcer covering at least $^1/_3$ of the cornea, defined as Keratomalacia.
- Corneal scarring.

It is vital to realize that many patients especially children who are vitamin A deficient will not have these documented ocular signs. This means that patients with the ocular signs are only the tip of the iceberg; there will be many others in the community who are vitamin A deficient but still have apparently normal eyes. Objective of this research study was to document a diagnostic sign which can identify vitamin A deficiency in its initial stage before irreversible and irreparable damage was done.

MATERIAL AND METHODS

This prospective case series study was conducted from September 1999 to September 2014 at ophthalmology department Chandka medical college and Syed eye clinic, Larkana, Pakistan. Patients identified clinically as cases of hypovitaminosis A on the basis of presence of "Imtiaz's sign", were included in the study during this period. Imtiaz's sign Fig. 1 was described by Professor Syed Imtiaz Ali Shah in Pakistan,[14] who explained that the staining of a dot or few dots of nasal or mostly temporal conjunctiva with surma (eyelash dye used for religious belief in men, women and children particularly in Muslims) or kajal (eyelash dye used for cosmetic purpose) indicates early / subclinical stage of Vitamin A deficiency. Patients with Retinitis pigmentosa, Glaucoma, chronic liver disease and malabsorption syndrome were excluded from the study. Associated symptoms and signs of vitamin A deficiency were noted. Relevant laboratory investigations available were also done on selected patients for the assessment of Vitamin A deficiency like, serum iron level, serum albumin level and LFT (Liver function tests). Serum retinol level (vitamin A level) was very costly and not available in many countries including Pakistan and serum RBP (Retinol binding protein) level was relatively less costly but was also not available in Pakistan. Dark adaptation threshold and X-ray of long bones to determine excessive deposition of periosteal bone were also performed. Patients were given therapeutic doses of vitamin A (2000 to 8000 IU daily in children and 10000 IU daily in adults) orally and improvement was observed. Resolution of symptoms or signs, including Imtiaz's sign of vitamin A deficiency was taken as a therapeutic test.

RESULTS

650 patients, 152 (23.38%) males and 498 (76.62%) females (Fig. 2) were identified as cases of hypovitaminosis A on the basis of presence of Imtiaz's sign. Age of the patients ranged from 5 years to 43 years and the mean age (± standard deviation) was 18.15 ± 10.20 years. Patients were divided into four different age groups (Fig. 3 and Table 1), 156 (24%) patients belonged to the 5 – 10 years age group. 299 (46%) patients were in the age group of 11-20 years, 88 (13.54%) patients were in the 21 – 30 years age group and 107 (16.46%) patients were in the 31 – 43 years age group. All patients replied positively for nyctalopia; however other signs (e.g. Conjunctival xerosis, Bitot's spots, Corneal xerosis, Keratomalacia, Corneal scarring), except Imtiaz's sign, were not observed due to the early stage of vitamin A deficiency. Relevant laboratory investigations were performed in 81 patients, 37 (45.68%) of them showed iron deficiency, 33 (40.74%) of them had hypoalbuminemia and 11 (13.58%) of them had disturbed LFTs (Fig 4). This shows that most of the patients suffering from vitamin A deficiency were victims of malnourishment.

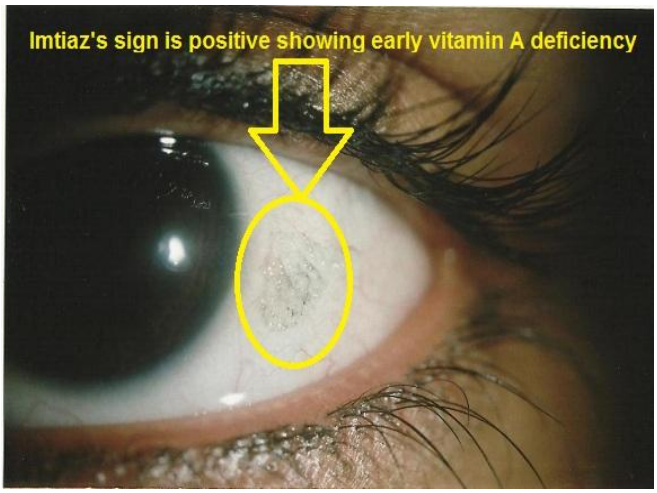

Fig. 1: Imtiaz's Sign.

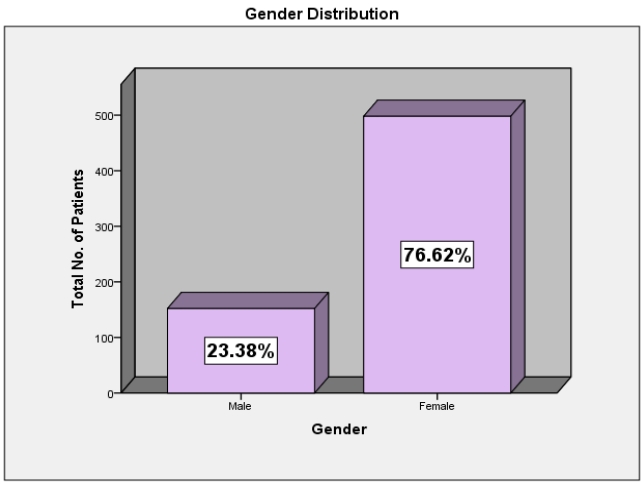

Fig. 2: Gender Distribution.

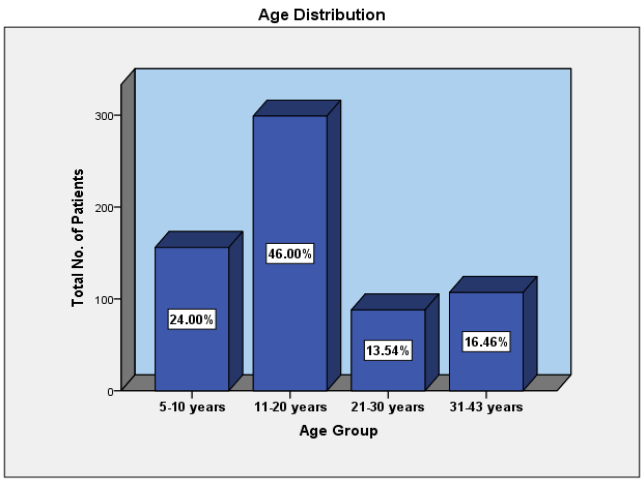

Fig. 3: Age Distribution.

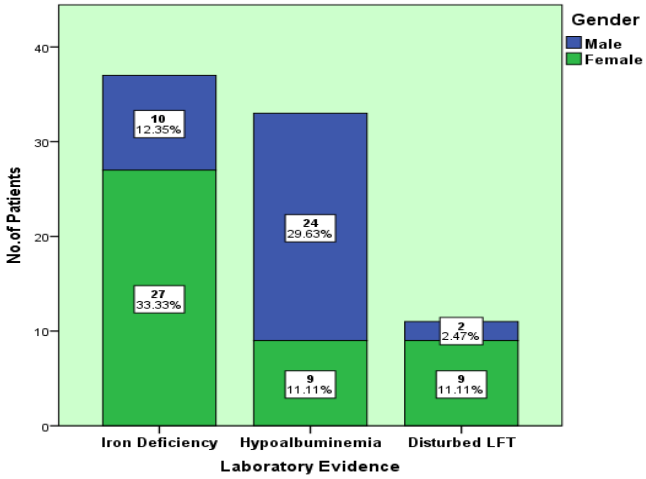

Fig. 4: Laboratory investigations.

Table 1:

Age Group	Male n (%)	Female n (%)	Total n (%)
5 - 10 years	48 (7.38)	108 (16.62)	156 (24)
11 - 20 years	59 (9.08)	240 (36.92)	299 (46)
21 - 30 years	19 (2.92)	69 (10.62)	88 (13.54)
31 - 43 years	26 (4.00)	81 (12.46)	107 (16.46)
Total	152 (23.38)	498 (76.62)	650 (100)

DISCUSSION

Estimates show that 1.02 billion people in the world are severely affected by micronutrient deficiencies and vitamin A is the most deficient nutrient in the body.[6] Xerophthalmia and Keratomalacia are recognized as chronic manifestations of severe deficiency of vitamin A[12]. Xerophthalmia is the leading cause of preventable childhood blindness with its earliest manifestations known are night blindness and Bitot's spots, followed by blinding keratomalacia[13]. According to WHO, 140 - 250 million children are at risk of vitamin A deficiency disorders (VADD) and increased morbidity and mortality even in the absence of ocular signs[8]. Therefore better signs for assessing vitamin A status are needed to identify vitamin A deficiency at an early stage. Bitot's spots are the buildup of Keratin located superficially in the conjunctiva usually in the form of triangular foamy lesion with base towards limbus. In 1863, Pierre Bitot (1822 - 1888), a French physician, first described these spots in debilitated orphans.[9] Since then these spots have turned into the hallmark ocular sign of hypovitaminosis A. But several studies

suggest that administration of Vitamin A fails to abolish these spots[10,11] and permanent damage to the body tissues occur if delay in diagnosis is allowed for appearance of Bitot's spots. Imtiaz's sign is the staining of a dot or few dots of conjunctiva with surma or kajal and is the earliest diagnostic sign of vitamin A deficiency. Due to sub clinical deficiency of vitamin A rough areas of conjunctiva are produced which get the natural stain of kajal or surma used for cosmetic or religious purpose. These patients who are in the early phase of vitamin A deficiency often confirm visual difficulty in dim light reacting to a leading question, which indicates forthcoming nyctalopia. Administration of dietary or therapeutic supplements of vitamin A quickly resolves these stained areas and also resolves associated symptoms of vitamin A deficiency.

CONCLUSION

Due to non-availability of specific laboratory tests to assess vitamin A levels in the blood in most of the countries across the world, presence of an early and effective clinical diagnostic sign is desirable to avoid morbidity and mortality related to vitamin A deficiency. Imtiaz's sign is the diagnostic sign to identify vitamin A deficiency in its initial stage, when the sign and symptoms are reversible. Imtiaz's sign requires no costly tools for application, is safe and can be easily recognized and confirmed by therapeutic test of Vitamin A supplements.

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Revised the manuscript and reviewed the images.

Dr. Shahid Jamal Siddiqui
Substantial contribution to conception and design, acquisition of data or analysis and interpretation of data.

Dr. Safdar Ali Abbasi
Involved in drafting the manuscript and revising it critically.

Dr. Shabir Ahmad Bhutto
Final approval of the study to be published.

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