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Research Article

Prevalence Allusions of Albright's Hereditary Osteodystrophy Syndrome in South Asia

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Abstract

Albright's Hereditary Osteodystrophy (AHO) is a rare, complex genetic metabolic disorder that was first delineated by American endocrinologist Fuller Albright in 1942. This syndrome is characterized by physical features such as short stature, abnormal finger and toe bones, skin ossification, obesity, rounded facial appearance, flat nasal bridge, and in some cases, developmental and mental abnormalities. AHO is classified as a subtype of pseudohypoparathyroidism type 1A due to its association with resistance to parathyroid hormone. When AHO is inherited from parents, it leads to the development of the syndrome without hormonal issues, resulting in a condition known as Pseudo-Pseudo Hypoparathyroidism (PPHP).

PPHP is inherited in an autosomal dominant manner, caused by a mutation in the GNAS gene. This gene is responsible for producing a subunit of a protein called a G protein, which regulates the activity and production of specific hormones, including parathyroid hormone. Globally, AHO is considered a rare syndrome, with a prevalence of 0.7 in 100 individuals. It is further classified into subtypes 1a, 1b, 1c, and 2 based on different phenotypes and underlying mechanisms.

However, the purpose of this study is to investigate the rarity of the syndrome in the Asian subcontinent, specifically examining its prevalence, recent trends, and awareness within the selected demographic population. A survey-based approach was employed to gather data from several Asian countries. The findings of this study revealed significant variations in terms of gender distribution, family history, associated complications, Gs alpha subunit deficiency, and the age at which individuals are diagnosed with the syndrome. These variations underscore the need for a versatile approach to accurately diagnose and promptly treat individuals at risk of or already affected by the syndrome.

Keywords: Albright's hereditary osteodystrophy; X-linked dominant disorder; Autosomal dominant trait; Gs alpha subunit deficiency; South Asian countries.

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Introduction

Albright's Hereditary Osteodystrophy (AHO) syndrome, characterized by distinct physical features such as short stature, round face, flat nasal bridge, obesity, short neck, and brachydactyly, has been the subject of numerous genetic studies. These studies have consistently identified mutations in the GNAS1 gene as the underlying cause of the syndrome [1]. Historically, there have been conflicting reports regarding the prevalence of AHO in different genders. Earlier studies suggested a higher frequency in females compared to males, while recent reviews have challenged this finding and indicated a more balanced occurrence between the sexes [2]. Further investigations by Farfel, et al., revealed that patients with Pseudohypoparathyroidism type I (PHP I) and AHO exhibited abnormally low urinary cyclic adenosine monophosphate (cAMP) levels in response to parathyroid hormone (PTH) infusion. Researchers also observed a significant reduction in the activity of the G protein, referred to as 'N,' which plays a crucial role in linking the hormone receptor to adenylate cyclase. In subsequent studies, Farfel, et al., described typical features of PHP type Ia, including short stature, brachydactyly, hypocalcemia, elevated serum PTH levels, and decreased urinary cAMP excretion following PTH administration. Researchers noted a 50% decrease in erythrocyte Gs activity in PHP type I patients, but normal levels in clinically normal relatives [3]. Additionally, Bourne, et al., reported reduced red blood cell N protein activity by 40% in five patients with PHP type I. Notably, individuals with Pseudo-Pseudo Hypoparathyroidism (PPHP) exhibit the characteristic features of AHO without endocrine abnormalities. Researchers display a normal cellular cAMP response to PTH infusion, decreased erythrocyte Gs activity, and a GNAS1 mutation inherited from the father [4]. In contrast, patients with PHP type Ib (PHP1B) show renal resistance to PTH, decreased cAMP response to PTH infusion, normal erythrocyte Gs activity, and imprinting/methylation defects at the GNAS locus, resulting in the absence of maternal allele expression in renal tissue. While classic AHO features are typically absent in PHP1B, some cases have reported AHO-like characteristics. Although PHP1B does not involve generalized hormone resistance, there have been reports of resistance to thyroid-stimulating hormone (TSH) [5]. Furthermore, Mariot, et al., highlighted rare cases where patients with PHP1B exhibited AHO features due to decreased expression of G-alpha-s caused by epimutations at the GNAS locus [6]. In terms of prevalence, specific data regarding Albright's Hereditary Osteodystrophy in South Asia are limited. Due to the rarity of the syndrome, it is challenging to determine its exact prevalence in any particular region or country. However, it is reasonable to assume that the prevalence in South Asia would be consistent with the global estimates.

Objectives

i. The basic objective of this survey was to estimate the prevalence of Abright's Hereditary Osteodystrophy syndrome (AHOS) in South Asian countries.
ii. To provide insights, recent trends and epidemiology of the syndrome.
iii. To reach populations affected.

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iv. To develop and promote awareness.
v. To attest the aberrant and confirm the report on the Abright's Hereditary Osteodystrophy syndrome.
vi. To provide a statistical and prevalence report of Albright's Hereditary Osteodystrophy syndrome.
vii. To provide reference information to the public, researchers, and particularly to biomedical workers in order to be used as a magical key formula in the treatment and management of such rare autosomal hereditary disorders.

Methods

The project was conducted in a survey configuration; based on Questionnaire type, through selection of average countries in Asia. Also, it was made in form of an online Annexure (https://tinyurl.com/PAAHOS) and been filled by the participants from South Asian countries, which was the designated demographical area of the project. The data was collected by asking questions to the people whom author thought to have desired information related to this Hereditary syndrome. A formal list of questionnaires was prepared as it was aforementioned. And for the most part of it the author used a non-disguised approach. The participants involved or the respondents were asked questions on the demographic interest opinion.

Results

There was significant variation in the survey findings in terms of gender, family history, associated complications, association with Gs alpha subunit deficiency, and age of detection with the syndrome. According to the survey, in the total population percentage of the participants, only 21% are aware about Albright's Hereditary Osteodystrophy syndrome. And this is indicating the wide gap in the rate of awareness of this debilitating rare hereditary syndrome.

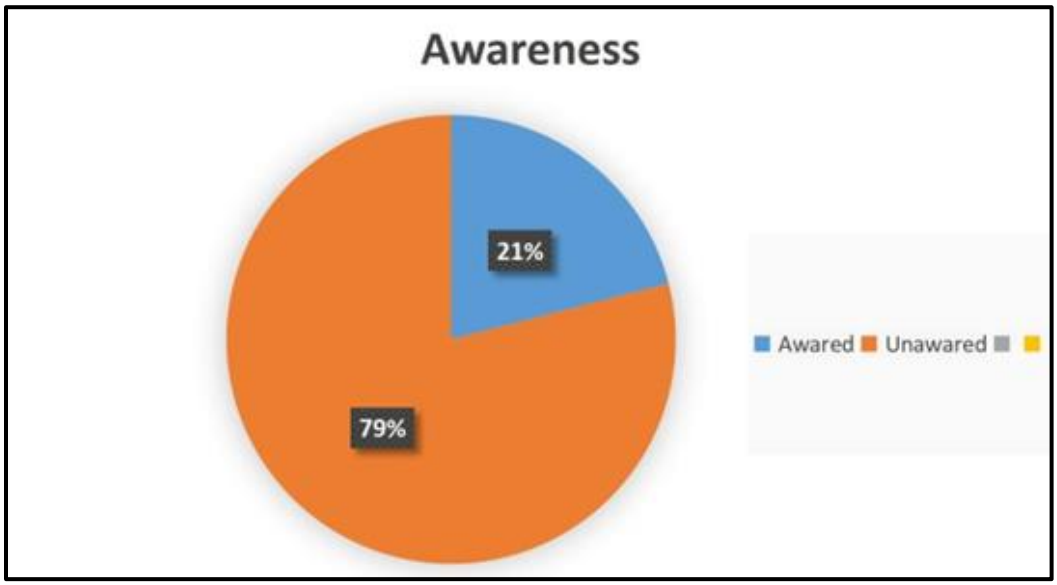

Figure 1: Percentage of Awareness in the population.

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The syndrome was originally thought to be transmitted as an X-linked dominant disorder, most likely based on initial observations that females were affected twice as often as males, the percentage of the females which were outlined with the cases has been yonder to that of males, though the number of female respondents is more in the data collected;

♂, ♀, ⚧	No.	Percentage (%)
Males ♂	56	35.67%
Females ♀	90	57.32%
Non-binary ⚧	0	0.00%
Non-specified	11	7.00%

Table 1: Gender-wise distribution of the Respondents.

Out of the total reported in the survey, the country with a greater number of Albright's Hereditary Osteodystrophy Syndrome prevalence reference was found to be the one with 41%, however this may be due to the highest population and development in that particular country, has been graphically distributed below:

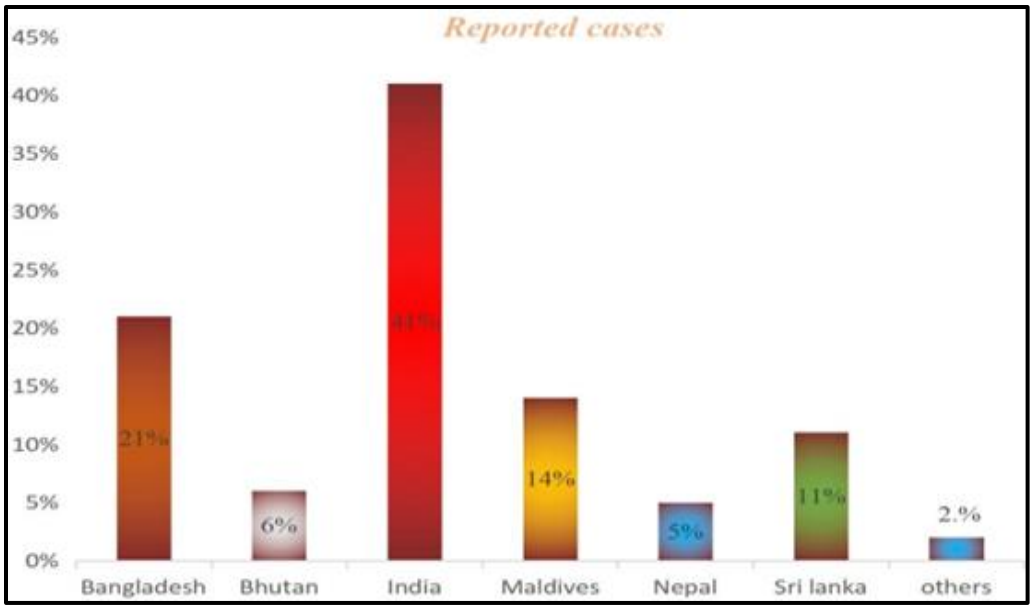

Figure 2: Country wise distribution of AHO.

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An individual may live with no signs of impairment to Albright's Hereditary Osteodystrophy Syndrome, but the risk of contracting an autosomal dominant trait of the syndrome may not be far off. However, it might be running on an individual very genetic system, waiting for triggers of an unhealthy lifestyle and neglected health concerns before displaying a striking development. Genetic health implications are a major concern for health professionals. That is why there is a need to an accurate account of the respondent's background through a family history question. This will help to identify a person's potential risks and, in doing so, it may help in proposing preventive measures on how to avoid inheriting the dangers of the parent's traits defects. Based on the collected data, 10 respondents were proclaiming to have the inheritance of the syndrome as it is graphically illustrated below:

Family history

Response	No. of respondents
YES (Inherited)	10
NO	89
Uncertain	58

Table 2: Family inheritance distribution.

Some of the respondents were not certain about the background of the syndrome in the family.

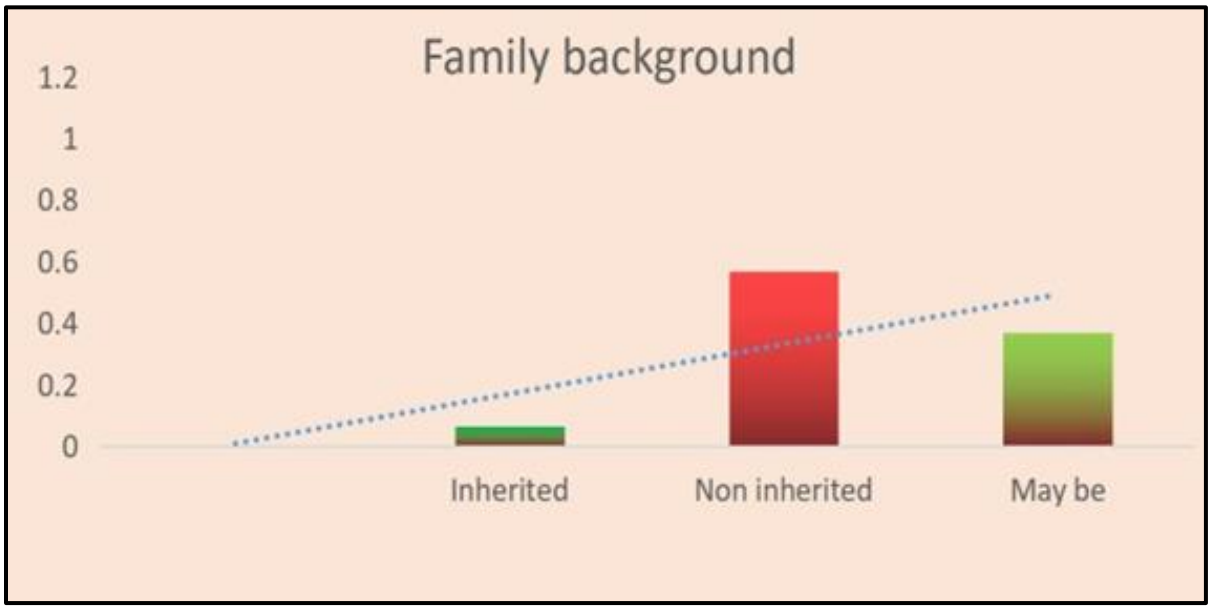

Figure 3: Family background distribution.

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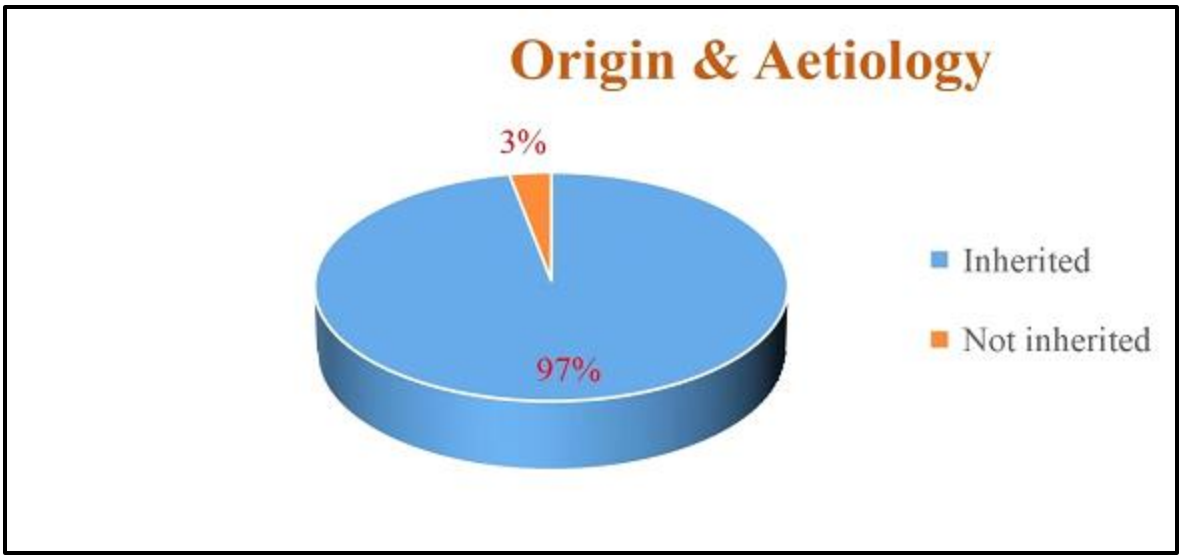

Figure 4: Origin and Aetiology.

Some of the respondent received prescription to some of the medications like Phosphate binders, supplementary Calcium and Vitamin D by the physician, howbeit, the variance is less as a history of medicational prescription received by an individual may have an effect in developing or not showing a sign of impairment.

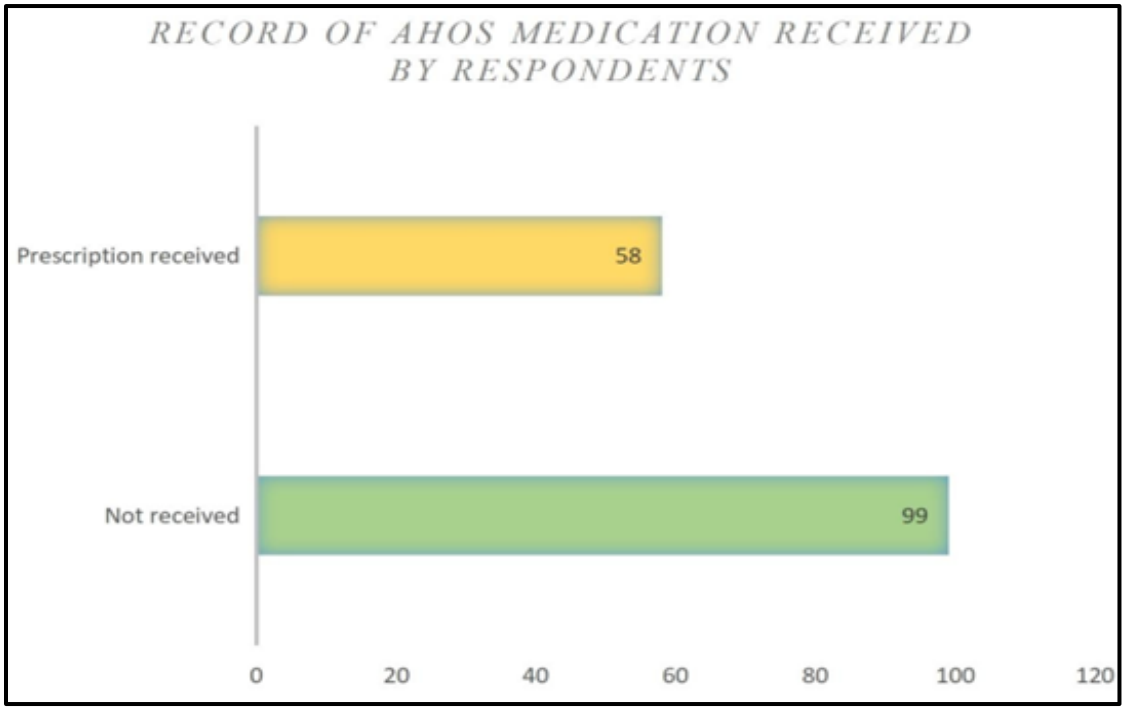

Figure 5: Medication therapy history distribution.

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The number of responded with the Gs alpha sub-unit deficiency was recorded to be 33.9% and those without the Gs alpha subunits 66.1%. The Gs alpha sub-unit (Gαs, Gsα) is a subunit of the heterotrimeric G protein Gs that stimulates the cAMP-dependent pathway by activating adenylyl cyclase. Gsα is a GTPase that functions as a cellular signaling protein. Gsα is the founding member of one of the four families of heterotrimeric G proteins [7].

Discussion

On appraising the information provided by this study, although limited in nature, it suggests a significant prevalence of Albright's Hereditary Osteodystrophy Syndrome in South Asia. The study focused on respondents from countries such as Bangladesh, Bhutan, India, Maldives, Nepal, Sri Lanka, and other nations in the region. This indicates that the prevalence of the syndrome in South Asia is notable, and it is likely to increase in the future. Therefore, raising awareness about the syndrome is crucial, and concerted efforts from public health workers, genetic counselors, endocrinologists, geneticists, and other healthcare professionals are necessary to develop effective strategies for managing the disorder and preventing its inheritance in future generations. It is important to note that global data on the prevalence of Albright's Hereditary Osteodystrophy is limited. However, a closely related disorder, Pseudohypoparathyroidism (PHP), has a prevalence ranging from 0.34 to 1.1 per 100,000 individuals. Although specific prevalence data for Albright's Hereditary Osteodystrophy is not available, it is estimated to be approximately 1 per 20,000 individuals [4].

Conclusion

In conclusion, the survey findings revealed significant variations in various aspects related to Albright's Hereditary Osteodystrophy Syndrome. The awareness about the syndrome among the population was found to be low, with only 21% of participants being aware of it. This highlights a substantial gap in knowledge regarding this debilitating rare hereditary syndrome. Regarding gender distribution, although the number of female respondents was higher, the percentage of reported cases was higher among males. The survey included participants from different countries in South Asia, and one particular country had the highest prevalence of Albright's Hereditary Osteodystrophy Syndrome, likely due to its larger population and development level. Understanding the family history and inheritance patterns is crucial in identifying potential risks and proposing preventive measures. Out of the respondents, 10 reported a family history of inheriting the syndrome, while others were uncertain or had no such history. Some respondents had received medication therapies such as phosphate binders, supplementary calcium, and vitamin D, which may have influenced the manifestation or absence of symptoms. In terms of Gs alpha subunit deficiency, 33.9% of respondents exhibited this condition, while the remaining 66.1% did not. The Gs alpha subunit plays a critical role in cellular signaling, specifically in the cAMP-dependent pathway. Although the study's data was limited, it suggests a significant prevalence of

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Albright's Hereditary Osteodystrophy Syndrome in South Asia. Raising awareness about the syndrome and implementing preventive measures is essential. The global prevalence of the syndrome remains uncertain, but related disorders like Pseudohypoparathyroidism have estimated prevalence rates. Further research and collaboration among healthcare professionals are needed to effectively manage the syndrome and prevent its inheritance in future generations.

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