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Seasonal variation and Vitamin-D status in ostensibly healthy Indian population: An experience from a tertiary care institute

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ABSTRACT

Background: 25-hydroxy vitamin-D (25(OH)D) deficiency is prevalent worldwide including India. Earlier some cross-sectional studies have discussed 25(OH)D deficiency and its prevalence. The correlation of 25(OH)D with seasonal variation has been reported rarely in India. To determine the 25(OH)D levels and seasonal changes of 25 (OH)D status at a tertiary care hospital in North-western India.

Materials and methods: 25(OH)D assessments performed in laboratories between 2018 and 2020 was acquired using hospital records. A total of 11,428 assays of serum 25(OH)D were analyzed in the study. Subjects were divided into three groups based on the International Endocrine Society's recommendation for serum 25(OH)D level. The 25(OH)D deficiency <20 ng/ml, insufficiency 20–29 ng/mL and sufficiency ≥30 ng/mL was defined. The months have been separated into the following seasons to analyze seasonal trends: Summer/monsoon (April–September), and winter/spring (October–March).

Results: The median 25(OH)D was 17.2 ng/mL. We observed the prevalence of 60 %, 24.1 % & 15.9 % of 25(OH) D deficiency, 25(OH)D insufficiency, and sufficiency respectively in the total number of individuals tested. 56 % male and 63 % females were 25(OH)D deficient. Notably, the lowest median 25(OH)D value was found in the 21–30 age group (14.8 ng/mL). A significant difference in 25(OH)D levels between the summer (18.7 ng/mL) and winter (15.8 ng/mL) seasons has been noticed.

Discussion: Current study revealing that 25(OH)D deficiency is common in all age groups and genders, according to our findings. Surprisingly, the lowest levels were reported in young adults. Seasonal variation has an impact on 25(OH)D status, however in all seasons 25(OH)D levels are lower than reference intervals. These findings suggest that the criteria for determining the state of 25(OH)D insufficiency and deficiency in the Indian population should be reconsidered.

1. Introduction

25(OH)D is a fat-soluble vitamin that is essential for human health. 25(OH)D is unique in that it can be absorbed as cholecalciferol (25(OH) D3) or ergocalciferol (25(OH)D2) in the diet, or it can be produced in the skin with appropriate sunshine exposure [1]. 25(OH)D is obtained through dietary sources as well as cutaneous biosynthesis under the influence of sunshine (80–90 %) [2]. 25(OH)D deficiency has been linked to rickets and osteomalacia in the past, and its impact on calcium metabolism has been extensively documented. Moreover, subsequent research has linked 25(OH)D to a variety of other disorders, including diabetes, metabolic syndrome, cardiovascular disease, autoimmune diseases like rheumatoid arthritis and Crohn's disease, infections like tuberculosis, and the risk of developing cancers of the breast, colon, ovary, and prostate [1,3,4].

25-hydroxyvitamin-D, the most prevalent circulating metabolite of

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Table 1
Vitamin D levels in Sufficient, Insufficient and Deficient category.

Vitamin D status	N	Percentage	Median	IQR
Deficient (<20 ng/mL)	5962	(60.0 %)	12.0	8.19–15.9
Insufficient (20–29 ng/mL)	2393	(24.1 %)	24.1	21.9–26.6
Sufficient (≥30 ng/mL)	1576	(15.9 %)	38.4	33.1–49.3

25(OH)D, is thought to be the most reliable and robust indicator of 25 (OH)D status [5]. 25(OH)D deficiency has been documented worldwide, in both sun-deprived and sun-rich areas. Despite the country's abundance of sunshine, Indian research consistently indicates poor 25(OH)D levels in numerous demographic studies [6–9]. Sun avoidance owing to fear of darkening, increasing skin pigmentation, clothing preferences, maximum time spent inside for occupational reasons, increased atmospheric pollution, and a lack of adequate dietary sources of 25(OH)D are all variables that contribute to this finding.

Because of its wide-ranging health effects, India's epidemic of 25 (OH)D deficiency is expected to add significantly to the immense burden on the healthcare system [9]. In previous studies conducted in India, researchers have found that 25(OH)D deficiency is widespread throughout the country, with prevalence rates varying from 70 % to 100 % of the Indian population [9]. However, in a huge country like India, where there are many distinct ethnicities, latitudes, customs, cultures, and attitudes, existing data on 25(OH)D status is insufficient and categorized in a multitude of ways, making analysis problematic [10]. Furthermore, across Europe, Latin America, North America, Asia, the Middle East, and Oceania, a seasonal variance in 25(OH)D levels and a significant tendency for hypovitaminosis D are higher in the winter months for all age groups [11]. The current hospital-based study was done to present information on the status of 25(OH)D in North Western India as well as seasonal variations.

2. Material & methods

The current retrospective study was carried out at a Tertiary health care Institute in Jodhpur, India, at the Department of Biochemistry. We obtained information on serum 25-hydroxyvitamin-D assay performed in clinical laboratory between April 2018 and March 2020. The data was collected from all age groups and both genders. Since the information was obtained from lab records, the medical history was recorded, and those who had diseases of the musculoskeletal system and connective tissue were excluded from the study. For analysis of seasonal variation, seasons were defined as - summer/monsoon (April to June; hot and dry; June to September; hot and wet); and winter/spring (October to March; cool and dry).

Serum 25-hydroxy Vitamin-D levels were determined in venous blood samples using the chemiluminescence immunoassay (CLIA) method on the DiaSorin analyser (DiaSorin LiaSon, Italy), which has a detection limit of 4.0–150 ng/mL. Internal and external quality control was performed on a regular basis, and the results were within the assay's recommended range. Subjects were divided into three groups based on the International Endocrine Society's recommendation for serum 25 (OH)D level [12]. 25(OH)D deficiency was diagnosed when the 25(OH) D level was less than 20 ng/ml, 2) 25(OH)D insufficiency was defined as a 25(OH)D level of 20–29 ng/mL and 3). 25(OH)D sufficiency was defined as a 25(OH)D levels ≥30 ng/mL.

The study was carried out in accordance with the Indian Council of Medical Research's standards and according to the approved protocol. After receiving approval from the institute's ethical committee, the data analysis procedure began. Informed permission was not necessary because this was a retrospective data-gathering project. During data entry and analysis, patient anonymity was protected.

The normality of the data was tested by the Kolmogrov-smirnov test. The study's findings were summarized as a median with an interquartile range and a percentage. To compare 25(OH)D levels between groups and seasons, a Mann-Whitney test was performed. Statistical significance was defined as a p-value of less than 0.05. The Statistical Package for the Social Sciences software was used to analyze the data.

Table 2a
Vitamin D levels in Male and female.

Gender	N	Median	IQR	P value
Male	4451 (44.8 %)	18.3	11.8–26.5	**<0.0001**
Female	5480 (55.2 %)	16.3	10.1–24.1	

Statistics test: Two-sample Wilcoxon rank-sum (Mann-Whitney) test, p value < 0.05 denoted as statistically significant.

3. Results

3.1. Median 25(OH)D levels in north-western Indian population

A total of 11,428 25(OH)D reports were evaluated in this retrospective study. Among them, 1497 (13 %) patients were excluded from our study as per exclusion criteria. The median 25(OH)D value was 17.2 ng/mL with 10.8–25.2 interquartile range.

On further analysis, based on 25(OH)D levels, the study population was categorized into three groups (Table 1). We have observed that 60 % population was having 25(OH)D deficiency (<20 ng/mL), 24 % were under 25(OH)D insufficiency (20–29 ng/mL) and only 15.9 % had sufficient 25(OH)D (≥30 ng/mL). The different 25(OH)D levels were observed among genders in this study (Table 2A). Lower 25(OH)D levels were found in female population when compared to male population which is statistically significant. Another interesting aspect among gender is the female population was higher than male population in this study.

3.2. Gender-wise 25(OH)D levels in different 25(OH)D categories

Table 2B shows the gender-wise 25(OH)D levels in different categories based on the 25(OH)D status. We observed that 56 % male population were deficient, 26 % were insufficient and 18 % were under sufficient category. Whereas in the female population 63 % were deficient, 23 % were insufficient and 14 % were under sufficient category. Among deficient category, the female population was higher than male population and the 25(OH)D levels are lower in females when compared to male population. However, in insufficient and sufficient categories there is no statistically significant difference in 25(OH)D levels.

Table 2b
Gender-wise Vitamin D levels in different Vitamin D categories.

Category	Male			Female			P value
	N	Median	IQR	N	Median	IQR	
Deficient (<20 ng/mL)	2505	12.7	8.7–16.2	3457	11.5	7.8–15.5	**<0.0001**
Insufficient (20–29 ng/mL)	1157	24.2	22–26.8	1236	23.8	21.9–26.4	0.0736
Sufficient (≥30 ng/mL)	789	38.3	32.9–48.3	787	38.7	33.3–50.1	0.1507

Statistics test: Two-sample Wilcoxon rank-sum (Mann-Whitney) test, p value < 0.05 denoted as statistically significant.

Table 3
Vitamin D levels in Paediatrics and Adults.

Group	N	Median	IQR	P value
Paediatrics (0y-12 y)	1394 (14.1 %)	18.5	11.6–27.1	**<0.0001**
Adult (13y-80y)	8534 (85.9 %)	16.9	10.6–24.9	

Statistics test: Two-sample Wilcoxon rank-sum (Mann-Whitney) test, p value < 0.05 denoted as statistically significant.

3.3. Age-wise 25(OH)D levels in both genders including pediatric and adults

The present study population, comprised of 14 % Pediatric group and 86 % adult age group. (Table 3). On this note, we have observed that 25 (OH)D value of pediatric group is higher than adult group which is statistically significant. We further divided our study population into age-wise subgroups (Table 4). Strangely we have observed that the lowest 25(OH)D value exists in 21–30 age group (14.8 ng/mL), and 31–40 age group (16.6 ng/mL). The difference between the age-wise subgroups 25(OH)D levels were statistically significant. In addition to this, the 25(OH)D levels difference in gender amongst age-wise subgroups analysis was done. 25(OH)D level difference between the genders in 11–20, 21–30, and 31–40 age groups (Table 4) was statistically significant. The female adolescent (11–20) and female young (21–30) age group were having lesser 25(OH)D levels in comparison to respective male age groups. Similarly, pediatric (6-10) age girls have lower 25 (OH)D levels than boys.

3.4. Seasonal variation of 25(OH)D

Fig. 1A shows the 25(OH)D levels of summer season and winter season among the population. The percentage of total tests of 25(OH)D is equal in both summer and winter seasons. In this study, significant difference of 25(OH)D levels between the summer season and winter season has been noticed. 25(OH)D levels in winter season are lesser than summer season which is statistically significant. In the current study, we have presented two consecutive seasons from 2018 summer to 2020 winter. In both consecutive years, the winter 25(OH)D levels were lesser which was statistically significant. (Table 5).

The seasonal variation of 25(OH)D data was further analyzed into deficient, insufficient, and sufficient categories. Among different subgroups, the deficient category population has shown a significant difference in 25(OH)D levels between summer and winter seasons (Fig. 1B), whereas insufficient and sufficient categories there is no statistically significant difference between the summer and winter seasons.

3.5. Monthly trend of 25(OH)D status

Fig. 2 shows the monthly median 25(OH)D trend in the year 2019-20. The highest 25(OH)D levels were observed in the months of August & September.

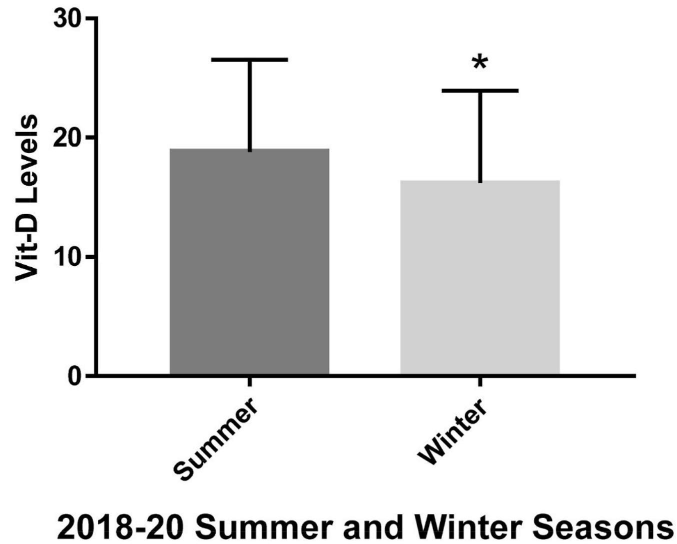

Fig. 1a. Vitamin-D levels in Summer and winter season of 2018-20.

4. Discussion

25(OH)D deficiency is well recognized as a significant health issue that affects not just musculoskeletal health but also a variety of acute and chronic disorders [13]. Diabetes, autoimmune disorders, certain malignancies, cardiovascular disease, cognitive decline, and difficult pregnancies have all been linked to low 25(OH)D levels [14]. Hypovitaminosis D is prevalent regardless of age, gender, occupation, rural/urban location, or regional distribution [7].

In the present retrospective study, the overall subject population median 25(OH)D is 17.2 ng/mL which indicates a deficient category. Only 16 % of subjects showed sufficient 25(OH)D levels and 60 % population was deficient. 25(OH)D deficiency is estimated to affect 20 to 80 percent of men and women in the United States, Canada, and Europe [15,16]. 25(OH)D deficiency is common in both adults and children in Asia and the Middle East [17]. Even within India, multiple studies from various parts of the nation show that roughly 70–90 percent of the population appears to be 25(OH)D deficient [9,18–20]. Since the majority of the participants in our study were from the middle to low socioeconomic groups, they were unaware of the importance of regular health screenings. Due to increased knowledge of the widespread incidence of 25(OH)D deficiency among various Indian communities, 25 (OH)D estimation is now one of the most commonly prescribed tests by Indian clinicians. We also found that 25(OH)D screening has increased in our study from first year to second year.

The prevalence of 25(OH)D deficiency in current study was observed to be 63 % in females and 56 % in males. In India, socioeconomic and social marginalization have a significant impact on women's nutritional status and food consumption. Previous research has shown that a

Table 4
Age-wise Vitamin D levels in different genders.

	Male			Female			
	N	Median	IQR	*N*	Median	IQR	P value
New born	*408*	17.3	10.5–27.9	*354*	15.8	10.1–24	0.1007
1-5	*215*	24.3	15.8–33.5	*110*	20.1	14–31.6	0.0940
6-10	*132*	20.5	15.1–28.1	*76*	16.1	10.9–22.8	**0.0013**
11-20	*382*	18.3	11.8–25.9	*347*	14.7	8.9–22.2	**<0.0001**
21-30	*894*	16.8	10.7–24.8	*1264*	13.4	8.4–21.3	**<0.0001**
31-40	*625*	17.3	11.6–24.8	*1082*	16.1	10.2–23.6	**0.0215**
41-50	*511*	17.6	11.8–25.4	*952*	17.5	10.9–24.8	0.4576
51-60	*595*	19.1	12.5–27.4	*703*	18.7	12–26.0	0.4245
>60	*687*	20.1	13.4–29.1	*585*	19.0	11.4–27.7	0.2377

Statistics test: Two-sample Wilcoxon rank-sum (Mann-Whitney) test, p value < 0.05 denoted as statistically significant.

Table 5
Vitamin D levels in summer and winter seasons year wise.

		Summer (April–September)	Winter (October–March)	p-value
2018–19	N	1182	2271	
	Median	19.2	15.2	<0.001
	25th-75th percentile	12.2–27.3	9.62–23.8	
2019–20	N	3786	2692	
	Median	18.4	15.8	<0.001
	25th-75th percentile	11.8–26.2	9.9–23.7	

Statistics test: Two-sample Wilcoxon rank-sum (Mann-Whitney) test, p value < 0.05 denoted as statistically significant.

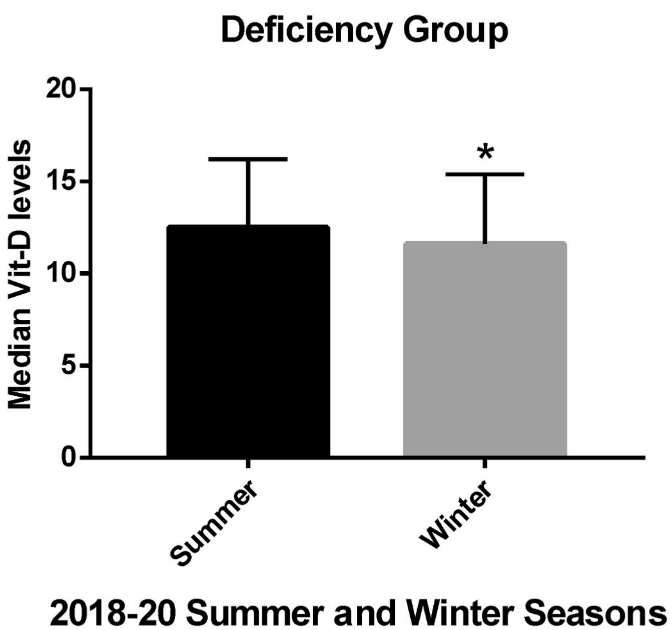

Fig. 1b. Vitamin-D levels in Summer and winter season in Deficiency group. Data was expressed in Median with IQR, and * indicates statistically significant ($p < 0.001$).

woman's nutritional status and consumption are influenced by factors such as her educational standing, family size, and the community to which she belongs. Between 2011 and 2014, Shukla et al. in India assessed serum 25(OH)D levels in 26,346 apparently healthy people who went to a private hospital for a normal health check-up [8]. They found 25(OH)D deficiency in 59 percent of the study participants (61 % males and 31 % females). Similarly, Sharma et al. also published data from a tertiary care hospital in north India, which included 5527 patients [4]. From 2011 to 2016, they observed 25(OH)D deficiency in 59.4 percent of the patients, with a declining trend. The prevalence in our analysis appears to be consistent with these studies, indicating that patients visiting this hospital had inadequate 25(OH)D levels. Moreover, this appears to be linked to a population-wide 25(OH)D deficiency.

According to the current study's age-based population analysis, 25 (OH)D deficiency and insufficiency were most prevalent among those aged 21 to 40. Furthermore, female adolescent and female early age participants had lower 25(OH)D levels than comparable male counterparts. Since the study was conducted in North-western India, where the majority of the population is vegetarian and 25(OH)D-rich dietary sources are limited and expensive for the socioeconomically marginalized groups, sun exposure is the sole major source of 25(OH)D. In that regard, the study conducted in Jodhpur, Rajasthan which is also called Suncity of India because the weather remains bright and sunny all around the year even though 25(OH)D deficiency is high. However, in a country like India, social and cultural taboos typically determine lifestyle habits such as the use of sunscreen creams, clothing (Ghoonghat especially in Rajasthan, Burkha in Muslim communities) which may reduce sun exposure, in addition to this vegetarianism-which restricts 25 (OH)D-rich diet options.

25(OH)D deficiency in adults was typically assumed to be limited to the geriatric, but the findings of current retrospective investigation demonstrated that 25(OH)D deficiency affects people of all ages. In our study we have observed the lower 25(OH)D levels in newborns, which shows that pregnant women have low supplementation of 25(OH)D. In a study by Shivane et al., 70 percent of 1137 individuals in the 25–35 age group had 25(OH)D levels below 20 ng/ml [21]. Similarly, 65.5 percent of females in the 30-year age group have been reported to be 25(OH)D deficient in a study by Garg et al. [22]. Even healthy young soldiers, as well as young sportswomen, were found to be 25(OH)D deficient despite adequate calcium consumption, sun exposure, and a regular exercise regimen [23,24].

From earlier studies, the amount of 25(OH)D in the body is directly

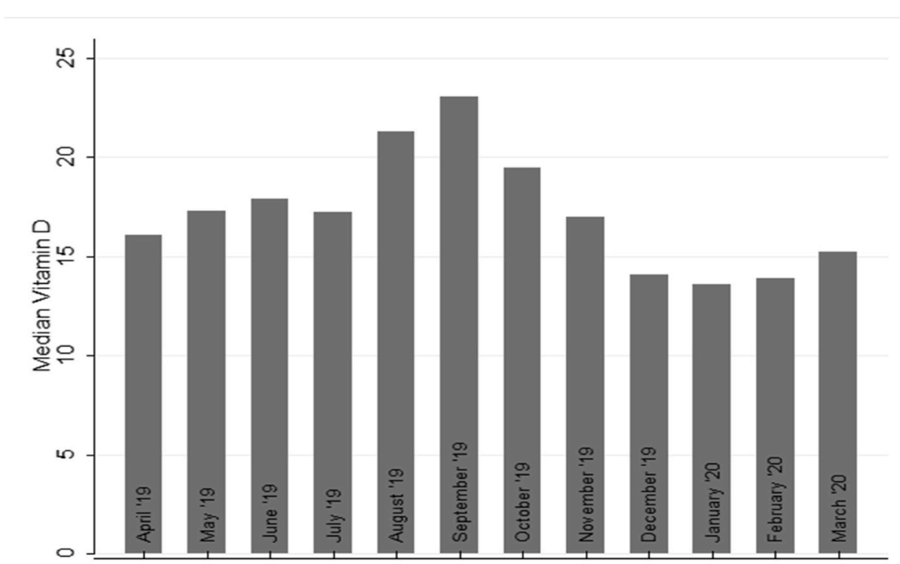

Fig. 2. Vitamin-D levels of monthly median level trend in the year of 2019-20.

proportional to the amount of time being spent in sunlight [9]. In comparison to countries nearer the poles, countries closer to the equator receive more sunlight annually, which varies with the seasons. As a result, both latitude and seasons have an impact on the amount of sunlight that a population can get. The data on seasonal variation in serum 25(OH)D levels is scanty in India. In a rural population in north India, Sahu et al. found that mean serum 25(OH)D levels were nearly twice as high in the summer as they were in the winter [25]. Similarly, serum 25(OH)D levels were considerably lower throughout the winter-spring seasons compared to the summer-autumn seasons in a hospital-based investigation by Shukla et al. [8]. The same result was reported in the current investigation, with 25(OH)D levels being significantly greater in the summer/autumn season during which the levels were towards the lower side of reference range. During the summer months, the seasonal fluctuations in serum 25(OH)D appear to reflect increased exposure to sunshine and increased 25(OH)D production. This is reflected in elevated serum 25(OH)D levels in the following season, in our case the monsoon, when peak levels were observed in August & September (Fig. 2). Winters had the lowest 25(OH)D levels, which is to be expected due to the fully covered clothes during wintertime since the increased solar zenith angle and less solar radiation.

5. Limitations of the study

Despite the substantial consequences of the present prevalence of 25 (OH)D deficiency, there are a few limitations in our research. Because the study samples came from patients at a tertiary care hospital, the findings cannot be extrapolated to a healthy population in the community. Hypervitaminosis has been detected in some subjects who were excluded from the study. We were also unable to examine the impact of unrecorded prior supplementation and confounding medical conditions on serum 25(OH)D levels because the data was derived from the hospital records of the biochemistry laboratory. The seasonality report is from cross-sectional data, not a comparison of paired samples in summer and winter.

6. Conclusion

The results of this study clearly indicated the significant incidence of 25(OH)D deficiency and insufficiency in the apparently healthy Indian population. We noted that 25(OH)D levels were higher in the summer/autumn season compared to the winter/spring season, while the levels were on the lower side of normal reference intervals in summer as well. In this context, the need of the hours is to undertake outcome studies that define deficiency, insufficiency, and optimal 25(OH)D levels in India based on hard clinical outcomes.

Disclosure of interest statement

Karli Sreenivasulu, Sojit Tomo, Kamalkant Shukla, Maithili karpaga Selvi, Mahendra Kumar Garg, Sumit Banerjee, Praveen Sharma, and Ravindra Shukla declare that they have no conflict of interest.

The authors declare no competing financial interests.

CRediT authorship contribution statement

Karli Sreenivasulu: Writing – original draft, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Mithu Banerjee:** Writing – review & editing, Validation, Supervision, Software, Resources, Project administration, Data curation, Conceptualization. **Sojit Tomo:** Visualization, Validation, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Kamalkant Shukla:** Validation, Methodology, Data curation. **Maithili Karpaga Selvi:** Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Mahendra Kumar Garg:** Supervision, Resources, Conceptualization. **Sumit Banerjee:** Resources, Methodology, Conceptualization. **Praveen Sharma:** Validation, Supervision, Conceptualization. **Ravindra Shukla:** Validation, Resources, Data curation, Conceptualization.

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