

## Vitamin A Level in Raised Intracranial Pressure in Children: A Cross-Sectional, Open-Label Study

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### Abstract

**Aims:** To study vitamin A level in pediatric patients with raised Intra Cranial Pressure (ICP).

**Settings and Design:** A cross-sectional, open-label study in the pediatric ward at Sir T G hospital and Government Medical College, Bhavnagar.

**Methods:** 30 patients in the age group of 2 months to 12 years admitted in the pediatric ward were included in the study during the period of 01/01/2015 to 30/08/2015. The subjects were selected based on having symptoms and signs suggestive of raised ICP. 15 subjects were selected as a control group from a pediatric outpatient without any major illness.

**Results:** 17 male and 13 female were enrolled in this study. 14/30 (46.6%) patients had low level (< 0.3 mg/L) of vitamin A, of which 9 were male and 5 were female; 7 patients (50%) belonged to the age group of 2 - 12 months; only 4/14 had any sign (dry skin) of vitamin A deficiency.

Out of 13 with raised ICP in infancy, 12 had bulging AF (7 low, 1 raised vitamin A level). Vomiting in 21 patients and convulsion in 19 was observed. 10/21 patients with vomiting had low vitamin A levels. The most common sign was neck stiffness. The most common diagnosis seen with raised ICP was pyogenic meningitis (16/30, eight had low vitamin A level). A total of 18 patients had abnormal Vitamin A levels, 14 had low and 4 had high (> 0.6 mg/L) levels.

In 15 control subjects, only one subject had low vitamin A level without any clinical manifestation of vitamin A deficiency, and rest had a normal level.

**Conclusion:** Abnormal levels of Vitamin A were seen in raised ICP in children including in infancy in 18/30 children; half 14/30 had low levels and 4/30 had high levels. 14/15 control had normal levels. Careful monitoring and administration of vitamin A is recommended in raised ICP in children.

**Keywords:** Raised ICP; Vitamin A Levels; Pyogenic Meningitis; Bulging AF; 2 Months to 12 Years; Convulsion; Vomiting; Bulging AF

### Introduction

Intracranial pressure (ICP) is derived from cerebral blood and cerebrospinal fluid (CSF) circulatory dynamics and can be affected in the course of many diseases of the central nervous system.  $(CSF) ICP = ICP_{vascular} + ICP_{CSF}$ . The vascular component [1,2] is difficult to express

quantitatively. More generally, multiple variables such as the arterial pressure, autoregulation, and cerebral venous outflow all contribute to the vascular component. The other circulatory CSF component may be expressed using Davson's equation [3]:  $ICP_{CSF} = (\text{resistance to CSF outflow}) \times (\text{CSF formation}) + (\text{pressure in sagittal sinus})$ . Any factor, which under physiological (for example, compression of jugular veins) or pathological conditions (brain swelling, space-occupying lesion, obstruction of CSF pathway) disturbs this circulation, may provoke an increase in ICP.

Cerebral perfusion pressure (CPP) represents the pressure gradient acting across the cerebrovascular bed and hence is an important factor in the regulation of the cerebral blood flow (CBF) [4]. Sufficient CPP is required to maintain a stable CBF. If the cerebral vessels are non-reactive, an increase in CPP may result in hyperemia, an increase in vasogenic edema, and a secondary increase in ICP [5,6]. Increased ICP signifies increased resistance to CSF outflow [7] or increased cerebral venous outflow pressure [8].

Vitamin A is one of the most important micronutrients affecting the health of children. It is necessary for orderly growth and differentiation of tissues [9,10].

Increased level of vitamin A is associated with raised intracranial pressure causing pseudotumor cerebri. Manifestations of central nervous system involvement are prominent, usually presenting with symptoms of raised intracranial pressure such as headache, vomiting, blurring of vision, diplopia, and papilloedema. Unbound serum or CSF vitamin A damages arachnoid granulations therefore drainage of CSF is impaired which may be a cause for raised ICP. Also increased CSF production and decreased drainage of CSF are possible mechanisms responsible for raised ICP.

Likewise, a low level of vitamin A is also found to be associated with raised intracranial pressure; a possible mechanism is not well understood but can be increased CSF production or impaired absorption and drainage.

### Methods

30 patients in the age group of 2 months to 12 years admitted in the pediatrics ward of Sir. T G Hospital, Bhavnagar was included in the study irrespective of disease condition if they met with study criteria. 15 subjects were selected as a control group from a pediatric outpatient without raised ICP or major illness.

**Inclusion criteria:** Children in the age group from 2 months to 12 years of age with clinically defined raised intracranial pressure:

1. Headache
2. Nausea and vomiting
3. Blurring of vision
4. Any of the clinical sign neck rigidity or Kernig sign or Brudzinski sign
5. In case of children < 1 year of age bulging anterior fontanel.

### Exclusion criteria

1. The first two months of age will not be included in the study.
2. Patients who had received oral vitamin A as part of a national program in the last one month or vitamin A was given at the time of admission.

### Results

The study was carried out on 30 patients in the age group of 2 months - 12 years with raised intracranial pressure admitted in the pediatric ward in one of the tertiary care, teaching institute of Gujarat, Sir T Hospital and Govt. Medical College, Bhavnagar.

Out of 30, 17 male and 13 female patients (1.3:1) were analyzed for measurement of vitamin A level and its relation with raised intracranial pressure, a prospective cross-sectional, open-label study (Table 1).

Age	Male	Female	Total
2 - 12 months	6	7	13
1 to 6 yr	6	3	9
6 to 12 yr	5	3	8
Total	17	13	30

**Table 1:** Age and sex distribution.

14 (46.6%) out of 30 patients showed a low level of vitamin A, of which 9 (64.4%) were male and 5 (35.7%) were female (Table 2) For conversion (1 μmol/L = 28.6 μg/dL = 0.286 mg/L).

Gender	Vitamin A level (mg/L) and numbers					
	Low	n < 0.3	Normal	n 0.3 - 0.6	High	n > 0.6
Male	0.18	9	0.40	6	0.63	2
Female	0.16	5	0.38	6	0.63	2
Mean ± SD	0.17 ± 0.075		0.39 ± 0.083		0.63 ± 0.01	

**Table 2:** Vitamin A level gender wise with Mean/SD.

$X^2 = 0.6206, p 0.7332, Yates chi-square test, Df = 1.$

There is no significant association between age and Vitamin A levels. Out of 14 patients with a low level, 7 (50%) belonged to age < 1 year (excluding the first 2 months) (Table 3).

Age	Vitamin A level (mg/L) and numbers					
	Low < 0.3	n	Normal 0.3 - 0.6	N	High > 0.6	n
2 - 12 months	0.17	7	0.33	5	0.63	1
1 to 6 yr	0.16	5	0.41	3	0.64	1
6 to 12 yr	0.22	2	0.44	4	0.63	2
Mean ± SD	0.17 ± 0.075		0.39 ± 0.08		0.63 ± 0.012	

**Table 3:** Vitamin A level in different age group with Mean/SD.

$X^2 = 2.569, p 0.6324, Yates chi-square test, Df = 2.$

Out of 13 patients with raised ICP of infancy period, 11 patients have bulging AF of which 6 patients had a low vitamin A level (Table 4).

AF Status	Vitamin A level numbers			Total
	Normal	Low	High	
Bulge	4	6	1	11
Not Bulge	1	1	0	2
Total	5	7	1	13

**Table 4:** Vitamin A level in INFANCY and Anterior Fontanel AF.

$X^2 = 0.2701; p 0.8737; Yates chi-square test, Df = 2.$

The most common complaint was vomiting in 21 patients (10 with low levels), and the second most common was convulsion in 19 patients (11 normal, 6 low levels) (Table 5).

Symptom	Vitamin A level		
	Normal (n = 12)	Low (n = 14)	High (n = 4)
Vomiting	9	10	2
Convulsion	11	6	2
Poor feeding	3	6	0
Fever	5	2	1
Headache	4	1	0
Excessive crying	0	3	0
Altered sensorium	1	1	0

**Table 5:** Presenting complain and vitamin A level.

18 patients had neck stiffness (11 had normal, 5 low, and 2 high vitamin A levels). In the patient with low vitamin A level prominent sign was bulging anterior fontanel (AF) seen in 6 out of 14 patients (Table 6).

Clinical signs	Vitamin A level		
	Normal (n = 12)	Low (n = 14)	High (n = 4)
Neck stiffness	11	5	2
AF bulge	4	6	1
Kernig sign	7	5	2
Brudzinski sign	3	2	2

**Table 6:** Presenting signs and vitamin A level.

AF: Anterior Fontanel.

Table 7 shows the most common diagnosis seen with raised ICP was pyogenic meningitis in 16 patients of which 8 had low vitamin A levels. 14 patients with raised ICP had low vitamin A levels. 3 out of 6 cases of viral meningoencephalitis 3 had a low level of vitamin A.

Type of illness	Vitamin A level			Total
	Normal	Low	High	
Pyogenic meningitis	7	8	1	16
TB meningitis	4	3	1	8
Viral meningo-encephalitis	1	3	2	6
Total	12	14	4	30

**Table 7:** Vitamin A level and systemic disease.

$X^2 = 3.767; p 0.4517.$

There were 12 patients with raised ICP with undernutrition of whom, 6 had normal vitamin A, 4 had low and 2 had a high level. Out of 30 patients, 14 patients had low vitamin A levels; there was no clinical manifestation of vitamin A deficiency except 4 having dry skin (Table 8).

Diagnosis	Vitamin A level			Total
	Normal	Low	High	
Anemia	1	2	2	5
Undernutrition	6	2	4	12
Hydrocephalus	3	5	1	9
Infection (UTI/ URTI)	4	0	0	4

**Table 8:** Vitamin A level and other clinical condition.

UTI: Urinary Tract Infection; URTI: Upper Respiratory Tract Infection.

14 patients (out of 30 with raised ICP) had a low level of vitamin A and 4 had high levels; total 18 had abnormal Vitamin A levels; (Table 9).

Vitamin A level	Raised intracranial pressure ICP (30)
Normal	12
Abnormal	18
Low	14
High	4

**Table 9:** Vitamin A level and raised intracranial pressure.

In the control group having 15 children, only one child had borderline low vitamin A Level.

**Discussion**

The study was carried out on n = 30 patients in the age group of 2 months to 12 years who had raised intracranial pressure. Out of 30, 17 male and 13 female patients were analyzed for measurement of vitamin A level, maximum patients recorded in age up to 1 year (excluding the first 2 months) of age. Male/Female Ratio was 1.3: 1.

A study done at Tehran University of Medical Science [11], found a significant inverse association between serum levels of retinol and stunting in toddlers aged 10 - 36 months.

In the study done at University of Utah Health Science center, salt lake city, Utah 4 out of 28 subjects with raised ICP had normal vitamin A level and rest had high level while in our study there were 30 subjects; with 12 having normal vitamin A level, 14 having a low level, and only 4 having a high level [12].

Out of 13 patients in age group up to 1 year (excluding the first 2 months) 11 patients had bulging AF which is a sign of raised ICP. Out of these 11 patients with bulging AF, 6 had a low level of vitamin A and 4 had normal and 1 had a high level. This indicates some relation between vitamin A level and bulging AF with raised ICP.

One study from Israel described the association between pediatric pseudotumor cerebri and low serum vitamin A levels [13]. They retrospectively reviewed the charts of 6 children (5 boys, 1 girl; mean age 8 years) with increased intracranial pressure and low serum vitamin A levels. The etiology of vitamin A deficiency was a restricted diet (2 children), intestinal malabsorption caused by celiac disease (2 children), and undetermined cause (2 children). In conclusion, pseudotumor cerebri in children can be associated with vitamin A deficiency even when other manifestations of xerophthalmia do not exist. As our study involved a small sample size, applications of statistical test chi-square did not show any significant relation but needs further evaluation with a large sample size.

In the control group having 15 children, only one child had borderline low vitamin A Level.

### Conclusion

In the present study, most patients were in age up to 1 year excluding the first 2 months of life. Male/Female ratio is 1.3: 1. 14 patients (9 male) with raised ICP had low vitamin A levels. Out of 13 patients in age up to 1 year (excluding 2 months) with raised ICP, 7 had low vitamin A level. Out of 13 patients in age up to 1 year (excluding 2 months), 11 had a clinical sign of bulging AF of whom 6 had low vitamin A level. The most common presenting complaints were vomiting; (21 patients) of whom 10 had a low level of vitamin A. The most common presenting sign with raised ICP was neck stiffness (16 patients) of whom 5 had a low level. 16 patients were of pyogenic meningitis in which 8 had low vitamin A levels. In minor clinical condition with raised ICP, under-nutrition had no abnormality in vitamin A level. The second common condition seen is hydrocephalus in which 5 patients have a low level of vitamin A out of 9, which indicates some relation with bulging AF.

Finally, in my study sample size is 30 patients with raised ICP. Out of these 14 patients had low vitamin A levels and 4 had high vitamin A levels, so total is 18 patients with abnormal vitamin A levels, which is the most important finding, which needs further study with a large sample size for a precise result.

### Recommendation

Adequate dietary and supplemental vitamin A by food fortification should be provided to children [14].

Hypervitaminosis A causes damage to arachnoid granulations therefore drainage of CSF is impaired and this contributes to a rise in intracranial pressure. So, while prescribing vitamin A supplements to pediatric patients, appropriate dose and frequency should be adjusted and explained to relatives, to reduce chances of toxicities [15-17].

In the present study, 13 patients were from the infancy period from which 7 had low vitamin A levels; so, special dietary counseling and therapy should be given for the infancy period to prevent Vitamin A deficiency [18].

### What is already known?

Hypervitaminosis A causes pseudotumor cerebri (raised intracranial pressure).

### What is this study adds?

- Raised intracranial pressure ICP is associated with an abnormal level of vitamin A. Low level of vitamin A is more common with raised ICP than a high level.
- More infants were seen affected with raised ICP; and bulging AF sign was seen with raised ICP during the infancy period, in which low level of vitamin A was associated.
- Vomiting is a common presenting symptom and of whom half had low vitamin A levels.

### Declarations

The study was approved by the Institutional Review Board and Human Ethics Committee, and the scientific committee of the Govern-

ment Medical College, Bhavnagar, Guj India.

### Conflict of Interest

No conflict of interest.

### Funding

No financial grant was received for the study.

### Informed Consent

Consent was obtained in the local language from parents/guardians of the patients.

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