Revista de Chimie
https://revistadechimie.ro
https://doi.org/10.37358/Rev.Chim.1949

The Correlation of Vitamin D Level with Refractive Errors in Disabled Paediatric Patients

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Abstract: *Refractive errors are the most prevalent ocular disorders in paediatric ophthalmology having a higher occurrence in children with disabilities. This paper evaluated the refractive status of the disabled children and identified the influence of Vitamin D on this status. The study group was represented by 160 children (80 clinically healthy – group 0, 80 having different physical and/or mental disabilities – group 1) with ages between 5-16 years old, ophthalmologically examined between January 2019-January 2020. The prevalence of refractive errors was analysed according to the blood level of Vitamin D; the prevalence of the identified refractive errors was 35% in the group of children with disabilities (16% myopia, 14% astigmatism, 5% hyperopia) and 36% in the group of clinically healthy children (16% astigmatism, 10% myopia, 10% hyperopia). In group 1, an acceptable level (20-30 ng/mL) of Vitamin D was found in 61.54% of children with myopia, 25% in those with hyperopia, and 18.18% in those with astigmatism, the rest showing insufficiency of Vitamin D. Both children with disabilities/clinically healthy shown ocular refractive errors, the difference between the two groups being statistically insignificant (1%). The presence of Vitamin D in the blood in normal or insufficient levels suggests a strong correlation of its levels with the appearance of ocular refraction disorders.*

Keywords*: paediatric patients, disabled children, refractive errors, Vitamin D level*

1. Introduction

Worldwide, there are approximately 2.2 billion of people with visual disorders or blindness [1]. Approximately 1:3 person is diagnosed with a refractive error [2]. Among children, the most frequent causes of visual disorders are represented by uncorrected refractive errors, congenital cataract, retinopathy of prematurity, strabismus, amblyopia. Refractive errors are the most prevalent ocular disorders in paediatric pathology, having a much higher occurrence in children with disabilities [3,4]. Amblyopia is the bilateral or unilateral loss of sight, without any known cause, having a prevalence of up to 6.2% [5].

In Romania, the Law of social assistance no. 292/2011 (subsequently modified and completed through the Government Ordinance no. 31/2015), the Government Emergency Ordinance no. 34/2016, the Government Emergency Ordinance 82/2016, the Law no. 79/2017, the Law no. 110/2017 and the Law no. 194/2018 define the status and conditions of persons with disabilities [6,7]. The disability can be mental, of hearing, visual, physical or associated. From the diseases determining sensory deficiencies and the children's special needs, the following frequently met pathologies must be mentioned: Down

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syndrome, deafness, autism, attention-deficit/ hyperactivity disorder (ADHD) syndrome, cerebral paralysis etc. Children diagnosed with Down syndrome present an increased risk to develop or to be born with ocular pathologies (refractive errors, strabismus, blepharitis, nasolacrimal duct obstruction, cataract, keratoconus, ocular anomalies of anterior and posterior pole), their incidence being variable, 3-63 % [8-10]. The disorders of the retina have a prevalence between 1.7-40% [8], the frequency of the Brushfield spots being 36-81% [8]. Deafness is among the most important health problems that deeply affects the quality of life, having a prevalence of 1.4% among children with ages between 5 and 14 years [11]. An association between ocular pathologies and deafness negatively and deeply affects the communication and cognitive skills and thus in the case of these people, an ophthalmology screening is of crucial importance [12] in order to maximize their social and cognitive skills. The research carried out among the population with hearing impairment or deaf-mute has shown the fact that there is a prevalence of 35-57% of ocular problems [13]. ADHD represents one of the most frequent psychiatric affections diagnosed in children, having a worldwide prevalence of 5.3% [14], out of which a large number show refractive or ocular problems [15-17].

Epidemiological studies reveal the fact that there are risk factors, both genetic and environmental, that favour the appearance of refractive errors, especially myopia [18]. A frequently incriminated genetic cause is the presence of the gene represented by the receptor for Vitamin D (VDR gene) and the 18 myopia and high myopia loci (based on linkage analysis) [18,19]. Vitamin D gene polymorphism is associated with small-medium myopia in Caucasians [18]. Active Vitamin D (cholecalciferol) helps in preventing the skeletal disorders by maintaining a normal level of calcium and phosphorus in the blood [20], being the most potent human steroid hormone and the only vitamin that is formed with the help of ultraviolet rays [21, 22].

A recent study reveals the fact that the persons with myopia show a 20% lower level of serum Vitamin D, compared to the population that do not show refractive errors [23]. The toxic level of Vitamin D is >100 ng/mL, an optimal serum Vitamin D level is between 30-100 ng/mL (American Society of Endocrinology, 2011) [23,24], a normal level is considered to be between 20-30 ng/mL, insufficient level is considered to be between 12-20 ng/mL, and deficiency <12 ng/mL. Corroborated, the environmental factors (as reading for a long time, avoiding sun exposure) and the low level of Vitamin D increase the risk of myopia, being able to change the genetic risk. Also, Vitamin D plays an important role in preventing age-related macular degeneration [25-27] and other degenerative diseases.

This study aims to evaluate the refractive status of the children with disabilities (other than the ocular ones) and to identify the influence of Vitamin D in the appearance of refractive errors. Thus, attention must be focused on the existence of refractive errors among the paediatric population with special needs (and not only), because once discovered and treated, their quality of life can be remarkably improved.

2. Materials and Methods

In this research, it was analysed in cross-section a group of 160 children, examined at Private General Practice Elisantes Teola SRL, from Marghita, Bihor County, Romania; they were under study for 1 year, between January 2019 - January 2020. The criteria for children's selection in the study were as follows:

- Inclusion criteria: children with ages between 5 and 16 years old, at their first ophthalmological examination; in the case of Group 1 (80 children) – they had to be already diagnosed with at least one of the following pathologies: Down syndrome, autism, ADHD, deafness; in the case of Group 0 (the witness group, 80 children) – the children had to be perfectly healthy;
- Exclusion criteria: children wearing glasses (already known with refractive errors).

For all 160 children, blood samples were taken for Vitamin D measurement. The samples were collected at the laboratory of *Dr. Pop Mircea* Municipal Hospital, Marghita, Bihor County, Romania, at 09:00 a.m. Each sample consisted in 5 mL venous blood obtained by puncture from the median cubital vein (antecubital fossa), in a vacutainer without anticoagulant, with / without separating gel. The serum was separated by centrifugation. The sample volume was at least 1 mL serum. For the quantitative determination of Vitamin D, the serum level of 25-OH Vitamin D was measured by the immunochemical method with electro-chemiluminescent detection (measures total Vitamin D: Vitamin D3, Vitamin D2 and other hydroxylated metabolites of Vitamin D). The design of this study is depicted in Figure 1.

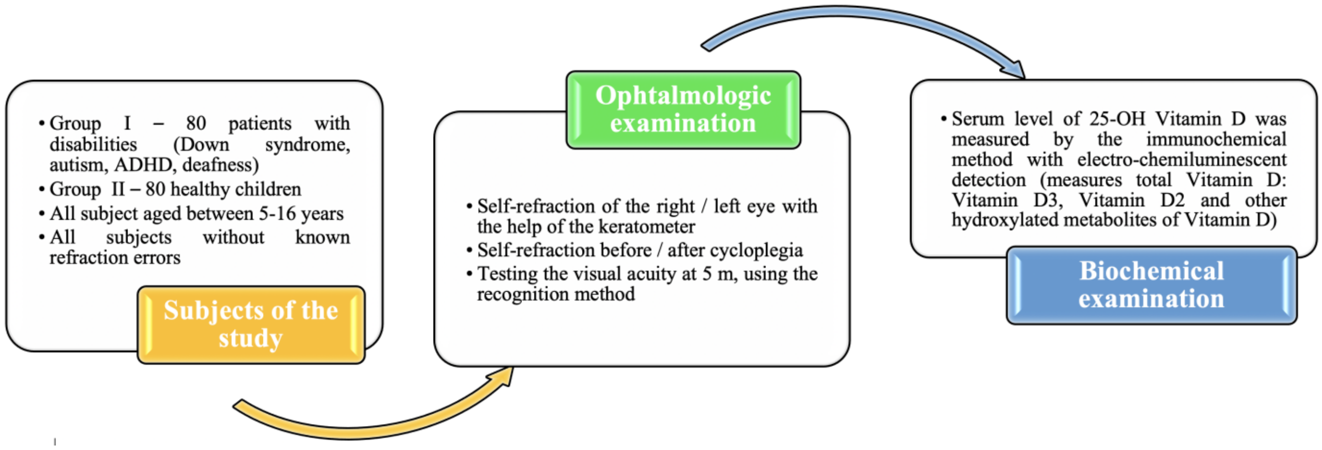

Figure 1. The study design

The biological reference range / UM from the laboratory: deficiency<12ng/mL; insufficient level 12-20 ng/mL; acceptable level 20-30 ng/mL; optimal level 30-100 ng/mL; toxic level>100 ng/mL. The status of Vitamin D in healthy children and adolescents is in line with the recommendations of the 2016, Global Consensus [28], which are similar to those advocated by the Paediatric Endocrine Society 2011 [24] and are based on serum 25–OH Vitamin D concentrations [29]. Relevant history regarding the type of disability, birth history, family history and history of consanguinity was recorded.

Ethical clearance was obtained from the SC ELISANTES TEOLA SRL din Marghita, no. 68/27.12.2018 and the study was conducted in accordance with the World Medical Association Code of Ethics – 1967, Declaration of Helsinki. The parents were informed regarding the stages of the study and have signed the participation agreement for each child concerning the dosing of Vitamin D.

For group 1, the children's diagnoses were established based on the specialty examinations and medical documents of each child, documents that have been provided by the family members (parents). Emmetropia was defined having a range between -0.25 to +0.25 diopters and a cylinder value no higher than -0.25 diopters; myopia was defined as a spherical equivalent of less than or equal to -0.5 diopter (<-0.5D), hyperopia as more than or equal to +0.5 diopter (≥+0.5D) and astigmatism as more than or equal to ±0.5 diopter (it was included the physiological astigmatism of ±0.5 and ±0.75). All children from both group 1 and group 0 have participated at the first ophthalmological examination.

The ophthalmological examination was performed in a room with a length of 5 m, in conditions of total obscurity and the procedure was fully explained to the parents who were present during the entire examination; also, it consisted of determining the self-refraction of the right and left eye with the help of the Canon Full Auto Ref-Keratometer RK-F2 (Canon INC Kawasaki, Japan, 2016), testing the visual acuity at 5 m using the recognition method (using the letter optotype and logMAR type E letters), without correction of the right eye (after occlusion of the left eye with black opaque occlusion), respectively of the left eye (after the previous occlusion of the right eye with the help of an opaque occlusion). Both eyes were instilled with cyclopentolate hydrochloride (SC Rompharm Company SRL, Romania) – one drop containing 0.3 mg active substance, 3 times at 5 min interval, at the bottom of the inferior conjunctival sac, after it was confirmed that no children had previously shown a history of seizures. In order to minimize the systematic absorption of the cyclopentolate, the occlusion of the inferior point of both eyes was carried out for 10 s; after 30 min of waiting, in order to carry out the complete cycloplegia from the moment of instillation of the first drop of cyclopentolate, the auto-refraction was measured again with the same refractometer mentioned above, at both right and left eyes.

The final results of this study are those obtained after cycloplegia. In the situation where it was necessary, for each case, the optic correction specific to each eye was realized with test lenses and the parent was given the optical medical prescription.

The statistical analysis of the data was gathered and carried out using Microsoft Excel 2010 and Biostat Programme 5.9.8.5. A $p<0.05$ value was considered the threshold of the statistical significance.

3. Results and discussions

The average age of the children in group 1 is 9.67±3.05 years, and that of the children in group 0 is 8.71±2.53 years, with a statistically significant difference $p<0.032$. Disabilities of children from study group 1 are presented in Table 1.

Table 1. The distribution of children from group 1 according to disabilities

Disability	Group 1 (n=80)	
	No.	%
Autism	13	16
Deafness	5	6
ADHD	2	3
Down syndrome	60	75

In the study group 1, cycloplegia was diagnosed in 80 children (100%), and for the same number of children in the witness group. 28 (35%) children from group 1 were identified with refractive problems like: myopia in 13 children (16%), hyperopia in 4 children (5%), and astigmatism in 11 children (14%), vs. 29 (36%) cases in the witness group, where myopia and hyperopia were equally identified in 8 children (10%) each and were exceeded by those with astigmatism, 13 children (16%), being necessary glasses prescription ($p=0.89$) with non-significant difference between the 2 groups of patients considered in the study. Table 2 shows that 103 (65.00%) children had not been identified with any refractive error, 52 from group 1 and 51 from group 0, statistically non-significant ($p=0.86$).

Table 2. Children who underwent cycloplegia, ametropia and amblyopes

Children' classification	Group 1		Group 0		p-value
	No.	%	No.	%	
Cycloplegia	80	100	80	100	1
Children with ametropia	28	35.00	29	36.00	0.89
No refractive error RE and/or LE*	52	65.00	51	63.75	0.86
Emmetropia RE and/or LE	45	56.25	47	58.75	0.74
Amblyopia	28	35.00	19	23.75	0.11
Myopia + amblyopia	8	10.00	1	1.25	0.01
Hyperopia + amblyopia	3	3.75	4	5.00	0.70
Astigmatism + amblyopia	10	12.50	10	12.50	1
Amblyopia without refractive error	7	8.75	4	7.50	0.77
Refractive error RE and/or LE without amblyopia	7	8.75	14	17.50	0.10

*RE – right eye; LE – left eye.

The majority of ametropic children in group 1 were myopic, followed by children with astigmatism and those with hyperopia. Amblyopia was statistically non-significant higher in group 1 (35% children vs. 23.75% children in the control group, p=0.11). The prevalence of myopia and amblyopia was found statistically significant higher in group 1 vs. group 0 (10% vs. 1.25%, p<0.01). Comparing the two groups, the prevalence of hyperopia and amblyopia was statistically non-significantly lower in group 1 (3.75% vs. 5.00% in group 0, p=0.70); the prevalence of astigmatism and amblyopia was equal in both groups; all of these children benefited from optical prescription. The rest of 7 children (8.75%) from group 1 and 4 children (7.50%) from group 0 (p=0.77) were categorized as having amblyopia, they were not identified with any refractive error and did not benefit of any optical prescription. A percentage of 8.75% children from group 1 and 17.50% children from group 0 diagnosed with refractive errors did not have amblyopia (p=0.10). There is also no significant statistical difference (p=0.74) between the two groups, concerning the number of children identified as emmetropic (56.25% vs. 58.75%).

As Table 3 shows, the percentage of children with myopia is higher in group 1, that of children with hyperopia is higher in group 0 and the percentage of children diagnosed with astigmatism is approximately the same in both groups, which emphasizes the need to carry out an ophthalmology screening among the population with disabilities of any kind.

Table 3. Percentage of children with refractive errors

Refractive error	Group 1	Group 0	p
	%		
Myopia	16	10	0.26
Hyperopia	5	10	0.2
Astigmatism	14	16	0.72
Total	35	36	0.89

For all the children, the blood value of Vitamin D was under 30 ng/mL (p<0.01); comparing group 1 and group 0, significant differences of Vitamin D values were obtained between the two groups for the acceptable, insufficient and deficiency level, p<0.01; there are significant differences regarding the ranges of Vitamin D values, with the predominance of small values in Group 1 as it is highlighted in Table 4. The mean value of Vitamin D for all the children taken in the study was 23.06±4.32, with a statistically significant lower mean value of this vitamin in group 1 (21.52±4.43 in group 1 vs 24.6±3.62. in the control group; p<0.01). Thus, is explained the acceptable value of Vitamin D having a lower prevalence in children with disabilities: 48 (60%) in group 1 vs. 72 (90%) in group 0, p<0.01. On the other hand, the insufficient level of this vitamin was significantly higher in disabled paediatric patients, 31(39%) in group 1 vs. 8 (10%) in group 0, p<0.01. Vitamin D deficiency was found only in one disabled infant. Thus, for this case, there were no statistically significant differences (p=0.37) (Table 4).

Table 4. Distribution of groups according to the level of dosed Vitamin D

Vitamin D value (ng/mL)		<12	12-20	20-30	Mean value	Standard deviation
Group 1	%	1	39	60	21.52	4.43
Group 0	%	0	10	90	24.6	3.62
Group 0+Group 1	%	1	24	75	23.06	4.32
p-value		0.37	<0.01	<0.01	<0.01	

From the total of 160 children, those with myopia represent 13%; out of these, an insufficient Vitamin D level (<20 ng/mL) is present in 28.57% vs. 24.26% (p=0.67) of cases without myopia, this data correlates with the literature findings. A percentage of 71.43 % children with myopia vs 75.54% children without myopia have a level of Vitamin D >20 ng/mL, considered as being acceptable. Hyperopia represents 8% from the total of 160 children from the two groups, from these, 75.00% having an acceptable value of Vitamin D equal to the prevalence of Vitamin D in children without hyperopia; this is secondary to the same amount of time exposure in sunlight combined with a more balanced diet. A percentage of 25.00% children with hyperopia and the same prevalence in children without hyperopia were identified with a level of Vitamin D <20 ng/mL, considered insufficient, statistically non-significant, with p=1. The paediatric patients included in this study that have been diagnosed with astigmatism represent 15% from the total of 160, from which 41.67% vs. 22.06% of those without astigmatism have a level of Vitamin D <20 ng/mL, (p=0.04), which means they show an insufficient level of Vitamin D, while 58.33% of children with astigmatism and 77.94% without astigmatism show an acceptable Vitamin D level between 20 -30 ng/mL(p=0.04) (Figure 2).

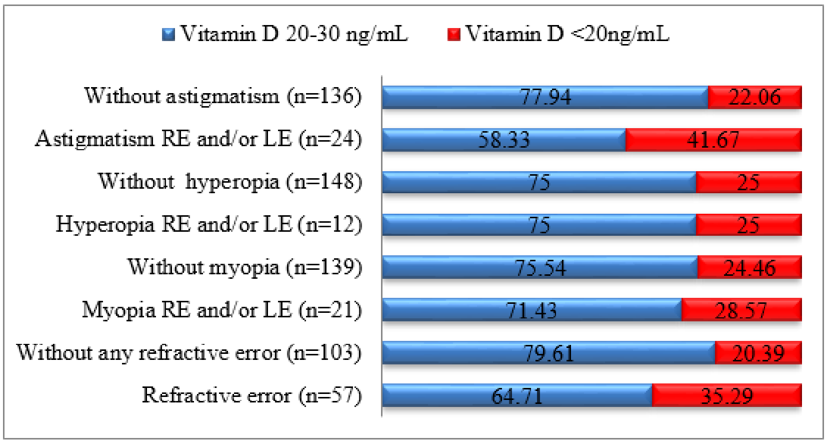

Figure 2. The percentage of children with / without refractive errors with an acceptable / insufficient level of Vitamin D

The distribution in Figure 2 shows that children without any refractive error have a statistically significant higher prevalence of the acceptable level of Vitamin D than those with refractive errors (79.61% in children without any refractive error vs. 64.71% in the group of children with refractive errors, p=0.04); the insufficient level of Vitamin D is statistically significant higher (p=0.04) in children with a refractive error (35.29%) vs. 20.39% in the group of children without any refractive error.

Figure 3 reveals that children with myopia have a lower prevalence of the acceptable level of Vitamin D in 61.54% cases in group 1 vs. 87.50% cases in group 0, being statistically insignificant (p=0.21); the insufficient level of Vitamin D has a higher prevalence in group 1 compared to group 0 (38.46% vs. 12.50%, p=0.21).

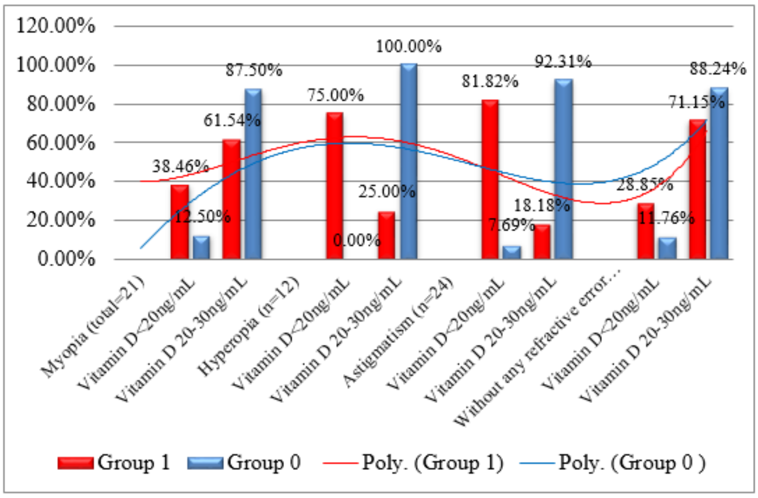

Figure 3. Vitamin D related to children with /without refractive errors according to groups

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https://doi.org/10.37358/Rev.Chim.1949

These data attest the early results from literature about the fact that myopia is more prevalent in children with low values of Vitamin D. The group of those with hyperopia and disabilities has shown a level of Vitamin D between 20-30 ng/mL in 25% of cases vs. 100% of cases in group 0, statistically significant (p=0.0068); the rest of 75% cases from group 1 had a level <20 ng/mL while no children with hyperopia was identified in the reference group with this value, being statistically significant (p=0.0068). From those with astigmatism and disabilities, 18.18% in group 1 have shown a level between 20 -30 ng/mL vs. 92.31% in group 0, p=0.003; the rest of 81.82% from group 1 and 7.69% from group 0 having Vitamin D deficiency, statistically significant (p=0.003).

The prevalence of insufficient Vitamin D value is statistically higher in the group of children with disabilities, indicating a possible association between its value and the development of refractive errors in this group. In the case of children without any refractive error was identified a statistically significant lower level of Vitamin D between 20-30 ng/mL in children with disabilities (71.15% cases in group 1 compared to 88.24% cases in group 0, p<0.01). The insufficiency of Vitamin D in children without any refractive error has a statistically significant correlation between groups (28.85% group 1 vs. 11.76% group 0, p<0.01).

The evaluation of a child with disabilities should always include a close examination of visual acuity, but also an ophthalmological examination and should be exactly the same as the one of a child without disabilities, considering also all the adaptations necessary to each disabled child, according and appropriate to his age and capacity to relate. The results of this study show the importance of ophthalmology screening among children with special needs, as the detection of refractive errors and automatically, their subsequent corrections will be extremely important for increasing the quality of life and preserving the social abilities of these children. Main findings of this research are summarised in Figure 4.

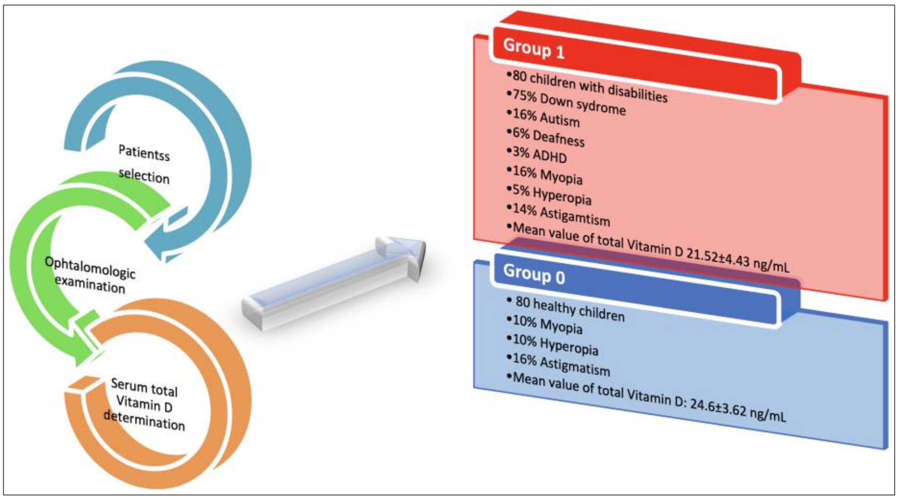

Figure 4. The main findings of this research

The inferior limit of 5 years old was chosen for the children participating in this study because children with a smaller age can be easily distracted by the environment. Children with disabilities are vulnerable and predisposed to social, professional, educational and medical neglect and rely to a great extent on their visual abilities in order to fulfil their daily tasks [14]. According to the studies presented in the literature data, they are more predisposed to the occurrence of refractive ocular problems, to a bigger extent than the clinically healthy children of the same age [30-33].

Our research shows that of 80 children with disabilities, the prevalence of 35% refractive error is similar to other studies shown in Table 5, indicating that the sequence among groups distributed worldwide are roughly the same. There were found myopia in 16% of cases, hyperopia in 5% of cases and astigmatism in 14% of disabled children while McQuaid and Arvidsson identified a prevalence of myopia in 11% of cases, 15% hyperopia and 12% astigmatism; Chang et al. found out myopia in 54% of cases and hyperopia in 3% of cases; Bankes identified 8% myopia, 27% hyperopia and 6% astigmatism [4,34,35]. The prevalence of myopia identified by other authors was higher in Asia [4]. Also, other studies conducted on children with disabilities, regarding the prevalence of ocular refraction disorders, are recorded in the specialized literature, some of them being presented in Table 5 [4, 33-39].

Table 5. The prevalence of refraction errors among children with disabilities, in different studies

Author(s)	Year	Ref.	Country of study	Subjects tested (no.)	Age (years)	Refractive errors %
Fletcher and Thompson	1961	[33]	USA	102	<18	29
McQuaid and Arvidsson	1992	[34]	Saudi Arabia	58	1-11	41
Bankes	1974	[35]	UK	137	unknown	53
Nielsen et al.	2005	[36]	Denmark	923	4-15	46.7
Chang et al.	2005	[4]	Taiwan	68	15-23	57
Gogate et al.	2007	[37]	India	664	<16	26.8
Woodhouse et al.	2010	[38]	UK	173	2-21	46.9
Ezeh et al.	2018	[39]	Nigeria	176	5-17	60
Current study	2018/2019		Romania	80	5-16	35

In this study, children with disabilities have a relatively high prevalence of refractive errors because they are genetically prone to all sorts of anomalies including the ocular ones, not rarely ametropia being the most prevalent ocular anomaly [4].

Health prevention programs should focus on children with disabilities because they are considered a category at high risk for ocular problems and mostly due to the fact that the prevalence of refractive errors is alike in both groups. This is of great importance, emphasizing the fact that also the disabled children need regular and thorough ophthalmic examination, and appropriate care of their eyes as much as they are prone to social distancing [7].

Our results shown that the prevalence of amblyopia among children with disabilities was found in 35% of cases, while none of the above authors of international studies [33-39] revealed any data about the prevalence of amblyopia or level of Vitamin D in the blood. This rate of 35% of children with amblyopia is higher than that of 2.8% identified by Mocanu and Horhad [40] in Romania and almost similar to that of 37.9% found in Australia [5]. In the group of clinically healthy children, 36% were identified with refractive errors, this rate being smaller than 55% identified in another study conducted by Hendrickson and Bleything [41]. Uncorrected refractive error in children with ages ranging from 5-15 years old remains the main cause of vision impairment, this problem being often unaddressed in many countries, as well as in Romania [41]. The prevalence of refractive errors is roughly the same in both groups of this research due to the increased time spent indoors combined with great amount of time doing near work, especially using smartphones, combined with the inappropriate diet that makes the insufficient Vitamin D values to mediate the appearance of ametropia [20,21].

Data from the literature highlight the association between myopia and the level of Vitamin D in the blood, but also the role of other vitamins (A, B, E, etc.), all of these substances (and many more others) having a decisive role in the visual acuity [24-26,42-44]. The Vitamin D deficiencies with an inappropriate diet, the lack of sufficient exposure to the sun, represent the favourable factors for the appearance of the decreased value of Vitamin D in the blood [45,46].

The mean value of Vitamin D for all the children taken in the study was 23.06±4.32 ng/mL and it is considered to be an acceptable level. Children can achieve this value because of the faster digitalization era we are living in, being prone to watch television, using computer, this resulting in the lack of motion and little exposure to natural light [17]. The reason why children with disabilities have a lower mean value of Vitamin D is that they have more specially designated indoor activities that prevent sun exposure and Vitamin D synthesis combined with an inadequate diet that prevents reaching an optimal level of this vitamin [24,27]. A higher mean value of Vitamin D was identified in the control group because they are more active, have a higher medium time of exposure to sunlight and a more balanced diet than children from the study group [23].

In a study conducted by Willem et al. (2011), 50.2% of children with myopia have shown an acceptable Vitamin D level in the blood (20-30 ng/mL) [47] vs 71.43% identified in the present study. There were not identified literature studies to show a direct correlation between the blood level of Vitamin D and the existence of other refractive errors besides myopia. Another study carried out by Choi et al. (2014), on a group of 2038 teenagers (between 13-18 years old) has identified the existence of a Vitamin D level <20 ng/mL, both in the group with myopia, and in that without myopia [47]. In the present study, there is an acceptable level and deficiency both in children with myopia, and in those without myopia (those with refractive errors). At the same time, another longitudinal study carried out by Morgan and Rose (2014) does not sustain the hypothesis according to which *"these analyses do not provide support for the hypothesis that elevation of Vitamin D levels is the mechanism by which spending time outdoors protects against myopia"* [48,49].

An increased prevalence of insufficient level of Vitamin D in children with myopia vs children without myopia pleads for the fact that a low serum level may increase the risk of myopia [18,19]. The higher level of acceptable Vitamin D value in non-myopic children from the present study correlates with a normal ocular refractive status found by Kwon et al. as well as by other researchers [22,50]. Mutti et al. also identified that children with no refractive error have higher blood values of Vitamin D compared to myopes [29]. The differences in the Vitamin D serum level is also a suggestive discovery for intrinsic inequality of Vitamin D metabolism amid children with myopia and those without myopia. Children without myopia may have a higher freedom in motion compared to myopic ones also due to the fact that the absence of a refractive error is encouraging in spending more time outdoors. Children with myopia enrolled in this study have a lower prevalence of an acceptable level of Vitamin D due to their diet combined with a lower time of sunlight exposure which correlates with the data from literature [45].

The fact that the acceptable and insufficient level of Vitamin D are the same for both groups with hyperopia in this study implies that they spend the same amount of time playing outside. A higher insufficient level of Vitamin D in the group of children with refractive errors (35.29% vs. 20.39% in the group of children with no refractive errors) suggests they have more indoor playing activities and near work duties. Children with no refractive errors have a higher prevalence of the acceptable level of Vitamin D compared to children with refractive errors, considering they are more sociable and have more outdoors activities, being exposed for a longer period to sunlight, combined with a mixed diet [22].

The limits of the present research reside in the fact that it was carried out on a relatively small group of 160 children (80 with disabilities + 80 healthy). It is not known for how long these children have had a refractive error. Before this study, they have not undergone an ophthalmology examination. Furthermore, there are no comparative results obtained from studies realized on children with disabilities from other geographical areas of Romania; this is why the present results were compared with other international studies, as well as with two studies carried out in Western part of Romania [40,46], but it is not recorded whether those children had a disability. Because of the limited age of the children from the hereby study and the specific location, the results cannot be considered nationally representative.

The fact that 35% from the total of 80 investigated children with disabilities need correction with glasses and that all of them have an acceptable level or even an insufficient level of Vitamin D, emphasizes the importance of screening carried out on children in due time, regardless of the fact that they are healthy or show disabilities, and the fact that the refractive status of children is inadequate.

4. Conclusions

Both the children with disabilities and those clinically healthy show ocular refractive errors and emmetropia, the difference between the two groups being statistically insignificant. The study pinpoints that the lower mean value of Vitamin D has a higher prevalence among children with disabilities and that those without any refractive error have a higher prevalence of the acceptable level of Vitamin D. An insufficient level of Vitamin D with a higher prevalence in the group of disabled children pleads for a possible association of the insufficiency with the manifestation of ocular refractive disorders under the form of astigmatism, myopia and hyperopia. It is necessary to carry out more elaborated studies regarding the ocular refractive errors corelated with the level of Vitamin D for the development of present ophthalmology practice guides, with the maximization of therapeutic results and thus to support mainly the disabled children.

The findings of the present study are important in promoting health and also for promoting child screening to detect the development of refractive errors correlated with the Vitamin D values. Also, it is relevant in promoting ophthalmologic screening among children with disabilities, because they are prone in approximately equal measure with clinically healthy children to develop refractive disorders.

Funding: This paper benefited from financial support through the project "SmartDoct - High quality programs for PhD students and postdoctoral researchers of the University of Oradea for increasing the relevance of research and innovation in the context of the regional economy", ID / Project code: 123008, co-financed by the European Social Fund through the Human Capital Operational Program 2014-2020.

References

1.***WORLD HEALTH ORGANIZATION. Blindness and vision impairment. Available online: https://www.who.int/news-room/fact-sheets/detail/blindness-and-visual-impairment (accessed on 20.01.2020).

2.DAS, M., SPOWART, K., CROSSLEY, S., DUTTON, G.N., Evidence that children with special needs all require visual assessment, *Arch. Dis. Child.*, **95**, 2010, 888-892. doi: 10.1136/adc.2009.159053.

3.PARARAJASEGARAM, R., Vision 2020-the right to sight: From strategies to action, *Am. J. Ophthalmol.*, **128,** 1999, 359-360.

4.CHANG, Y.S., SHIH, M.H., TSENG, S.H., CHENG, H.C., TENG, C.L., Ophthalmologic abnormalities in high school students with mental retardation in Taiwan, *J. Formos. Med. Assoc.*, **104**, 2005, 578-584.

5.PAI, A.S., ROSE, K.A., LEONE, J.F., SHARBINI, S., BURLUTSKY, G., VARMA, R., WONG, T.Y., MITCHELL, P., Amblyopia prevalence and risk factors in Australia preschool children, *Opthalmology*, **119**, 2012, 138-144.

6.***The Low of social assistance. Available online: http://anpd.gov.ro/web/despre-noi/legislatie/legi/. (accessed on 15.11.2019).

7.BUNGAU, S., TIT, D.M., POPA, V.-C., SABAU, A., CIOCA, G., Practices and attitudes regarding the employment of people with disabilities in Romania, *Quality – Access to success*, **20**(170), 2019, 154-159.

8.LIYANAGE, S., BARNES, J., The eye and Down’s syndrome, *Br. J. Hosp. Med*., **69,** 2008, 632-643. doi: 10.12968/hmed.2008.69.11.31686.

9.NICULA, C., NICULA, D., POP, R.N., Results at 7 years after cross-linking procedure in keratoconic patients (Les resultats a 7 ans apres la procedure de reticulation chez les patients atteints de keratocone), *J. Francais D'Ophthalmologie*, **40**(7), 2017, 535-541. doi: 10.1016/j.jfo.2017.03.003.

10.IONESCU, I.C., CORBU, C.G., TANASE, C., IONITA, G., NICULA, C., COVILTIR, V., POTOP, V., CONSTANTIN, M., CODRICI, E., et al., Overexpression of tear inflammmatory cytokines as additional findings in keratoconus patients and their first degree family members, *Mediators Inflamm*., **2018**, 2018, 4285268. doi: 10.1155/2018/4285268.

11.STEVENS, G., FLAXMAN, S., BRUNSKILL, E., MASCARENHAS, M., MATHERS, C.D., FINUCANE, M., Global burden of disease hearing loss expert G global and regional hearing impairment prevalence: an analysis of 42 studies in 29 countries, *Eur. J. Public Health*, **23,** 2013, 146-152. doi: 10.1093/eurpub/ckr176.

12.WOODRUFF, M.E., Differential effects of various causes of deafness on the eyes, refractive errors, and vision of children, *Am. J. Optom. Physiol. Opt*., **63(**8**)**, 1986, 668-675. DOI: 10.1097/00006324-198608000-00011.

13.REGENBOGEN, L., GODEL, V., Ocular deficiencies in deaf children, *J. Pediatr. Ophthalmol. Strabismus*, **22**(6), 1985, 231-233.
14.POLANCZYK, G., JENSEN, P., Epidemiologic considerations in attention deficit hyperactivity disorder: a review and update, *Child Adolesc. Psychiatr. Clin. N. Am*., **17**, 2008, 245-260.
15.BORSTING, E., ROUSE, M., CHU, R., Measuring ADHD behaviors in children with symptomatic accommodative dysfunction or convergence insufficiency: a preliminary study, *Optometry*, **76,** 2005, 588-592. doi:10.1177/1087054713511528.
16.GRONLUND, M.A., ARING, E., LANDGREN, M., HELLSTROM, A., Visual function and ocular features in children and adolescents with Attention Deficit Hyperactivity Disorder, with and without treatment with stimulants, *Eye*, **21**, 2007, 494-502. doi: 10.1038/sj.eye.6702240.
17.SILVA, A.P., FRERE, A.F., Virtual environment to quantify the influence of colour stimuli on the performance of tasks requiring attention, *Biomed. Eng. Online*, **10**, 2011, 74. https://doi.org/10.1371/journal.pone.0122119.
18.CONGDON, N., WANG, Y., SONG, Y., CHOI, K., ZHANG, M., ZHOU, Z., XIE, Z., LI, L., LIU, X., SHARMA, A., WU, B., LAM, D.S.C., Visual Disability, Visual Function, and Myopia among Rural Chinese Secondary School Children: The Xichang Pediatric Refractive Error Study (X-PRES) – Report 1 Clinical and Epidemiologic Research, *Invest. Ophth. Vis. Sci*., **49(**7), 2008, 2888-2894. doi: 10.1167/iovs.07-1160.
19.LI, J., ZHANG, Q. Insight into the molecular genetics of myopia. *Molecular vision*, **23**, 2017, 1048-1080.
20.DUMITRU, N., COCOLOS, A., CARAGHEORGHEOPOL, A., DUMITRACHE, C., BRATU, O.G., NEAGU, T.P., DIACONU, C.C., GHEMIGIAN, A., Collagen-the ultrastructural element of the bone matrix, *Rev. Chim*. **69**(7), 2018, 1706-1709.
21.MUTTI, D.O., COOPER, M.E., DRAGAN, E., Vitamin D receptor (VDR) and group-specific component (GC, vitamin D-binding protein) polymorphisms in myopia, *Invest. Ophthalmol. Vis. Sci.*, **52**, 2011, 3818-3824. doi: 10.1167/iovs.10-6534.
22.RICHERA, S.P., JOSEPH, J., PIZZIMENTIB, The importance of vitamin D in systemic and ocular wellness, *J. Optom*., **6(**3)**,** 2013, 124-133. doi: 10.1016/j.optom.2012.11.001.
23.MICHAEL, F., NEIL, H., BINKLEY, C., HEIKE, A., BISCHOFF-FERRARI, C., GORDON, M., HANLEY, D.A., HEANEY, R.P., MURAD, M.H., WEAVER C.M. Evaluation, Treatment, and Prevention of Vitamin D Deficiency: an Endocrine Society Clinical Practice Guideline. J. Clin. Endocrinol. Metab., **96**(7), 2011, 1911-1930. https://doi.org/10.1210/jc.2011-0385
24.MISRA, M., PACAUD, D., PETRYK, A., COLLETT-SOLBERG, P.F., KAPPY, M., Drug and Therapeutics Committee of the Lawson Wilkins Pediatric Endocrine Society. Vitamin D deficiency in children and its management: review of current knowledge and recommendations, *Pediatrics*, **122**(2), 2008, 398-417. doi: 10.1542/peds.2007-1894
25.BUNGAU, S.G., ABDEL-DAIM, M.M., TIT, D.M., GHANEM, E., SATO S., MARUYAMA-INOUE, M., YAMANE, S., KADONOSONO, K., Health benefits of polyphenols and carotenoids in age-related eye diseases, *Oxid. Med. Cell. Longev*., **2019**, 2019, ID 9783429. https://doi.org/10.1155/2019/9783429
26.ABDEL-DAIM, M.M., ZAKHARY, N.I., ALEYA, L., BUNGAU, S.G., BOHARA, R.A., SIDDIQI, N.J., Aging, metabolic, and degenerative disorders: Biomedical value of antioxidants, *Oxid. Med. Cell. Longev.*, **2018**, 2018, 2 pages. https://doi.org/10.1155/2018/2098123
27.ABDEL-DAIM, M.M., EL-TAWIL, O.S., BUNGAU, S.G., ATANASOV, A.G., Applications of antioxidants in metabolic disorders and degenerative diseases: Mechanistic approach, *Oxid. Med. Cell. Longev*., **2019**, 2019, 3 pages. https://doi.org/10.1155/2019/4179676
28.MUNNS, C.F., SHAW, N., KIELEY, M., SPECKER, B.L., THACHER, T.D., OZONO, K., MICHIGAMI, T., TIOSANO, D., MUGHAL, M.Z., et al., Global Consensus Recommendations on Prevention and Management of Nutritional Rickets, *J. Clin. Endocrinol. Metab*., **101**(2), 2016, 394-415. doi: 10.1210/jc.2015-2175

29.***Ministry of Health, Ghid din 9 august 2019 privind evaluarea și terapia deficitului de vitamină D la gravidă, nou-născut și copil (in English: Guide from August 9, 2019 on the evaluation and therapy of vitamin D deficiency in pregnant, new-born and child), Official Monitor no. 773 of September 24, 2019. Available online: http://legislatie.just.ro/Public/DetaliiDocument/218406 (accessed 28 February 2020)
20.MUTTI, D.O., MARKS, A.R., Blood levels of vitamin D in teens and young adults with myopia, *Optom. Vis. Sci*., **88**(3), 2011, 377-382. DOI: 10.1097/OPX.0b013e31820b0385.
31.OLADEJO, M.A., OLADEJO, S.A., Educating students with disabilities in Nigeria: Some challenges and policy implications, *Eur. J. Humanit. Soc. Sci*., **3**, 2011, 128-139.
32.ADEDAYO, O.A., SAMUEL, O.W., Ophthalmic manifestations of children with Down's syndrome in Port Harcourt, Nigeria, *Clin. Ophthalmol*., **6**, 2012, 1859-1864.
33.FLETCHER, M.C., THOMPSON, M.M., Eye abnormalities in the mentally defective, *Am. J. Ment. Defic*., **66**, 1961, 242-244.
34.MC QUAID, R.D., ARVIDSSON, J., Vision examination of children in Riyadh's handicapped children house, *J. Am. Optom. Assoc*., **63**, 1992, 262-265.
35.BANKES, J.L.K., Ocular problems of mentally handicapped children, *Aust. J. Ophthalmol*., **2**, 1974, 71-74.
36.NIELSEN, S.L., SKOV, L., JENSEN, H., Visual dysfunctions and ocular disorders in children with developmental delay. II. Aspects of refractive errors, strabismus and contrast sensitivity, *Acta Ophthalmol. Scand*., **85(2)**, 2007, 149-156.
37.GOGATE, P., SONEJI, F.R., KHARAT, J., DULERA, H., DESHPANDE, M., GILBERT, C. et al., Ocular disorders in children with learning disabilities in special education schools of Pune, India, *Indian J. Ophthalmol*., **59**, 2011, 223-228.
38.WOODHOUSE, J.M., DAVIES, N., MCAVINCHEY, A., RYAN, B., Ocular and visual status among children in special schools in Wales: the burden of unrecognised visual impairment, *Arch. Dis. Child*., **99**, 2014, 500-504.
39.EZEH, E.I., IBANGA, A.A., DUKE, R.E., Visual status of special needs children in special education schools in Calabar, Cross River State, Nigeria, *Niger Postgrad. Med. J*., **25**, 2018, 161-165.
40.MOCANU, V., HORHAT, R., Prevalence and Risk Factors of Amblyopia among Refractive Errors in an Eastern European Population, *Medicina*, **54**, 2018, 6. doi: 10.3390/medicina54010006.
41.HENDRICKSON, K., BLEYTHING, W., The visual profile of Romanian children and adults assessed through vision screenings, *Optometry*, **72(**6), 2001, 388-396.
42.WILLEM, J.L., TIDEMAN, J., POLLING, R., VOORTMAN, T., JADDOE, V.W.V., UITTERLINDEN, A.G., HOFMAN, A.G., VINGERLING, J.R., FRANCO, O.H., KLAVER, C.C.W., Low serum vitamin D is associated with axial length and risk of myopia in young children, *Eur. J. Epidemiol*., **31**, 2016, 491-499. doi: 10.1007/s10654-016-0128-8.
43.RAHDAR, A., TABOADA, P., HAJINEZHAD, M.R., BARANI, M., BEYZAEI, H., Effect of tocopherol on the properties of Pluronic F127 microemulsions: Physico-chemical characterization and in vivo toxicity. *J. Mol. Liq*., ***277***, 2019, 624-630.
44.RAHDAR, A., Effect of tocopherol on Pluronic microemulsions: turbidity studies and dynamic light scattering and dynamic surface tension measurements. *Nanomed. Res. J*., ***3***(4), 2018, 206-218.
45.EDWARDS, M.H., Do variations in normal nutrition play a role in the development of myopia?, *Optom. Vis. Sci*., **73(**10), 1996, 638-643. doi: 10.1097/00006324-199610000-00002.
46.STANESCU, A.M.A., GRAJDEANU, I.V., IANCU, M.A., PANTEA STOIAN, A., BRATU, O.G., SOCEA, B., SOCEA, L.I., DIACONU, C.C., Correlation of oral vitamin D administration with the severity of psoriasis and the presence of metabolic syndrome, *Rev. Chim*. **69**(7), 2018, 1668-1672.
47.CHOI, J.A., HAN, K., PARK, Y.M., LA T.Y., Low serum 25-hydroxyvitamin D is associated with myopia in Korean adolescents, *Invest. Ophth. Vis. Sci.*, **55**, 2014, 2041-2047. https://doi.org/10.1167/iovs.13-12853.

48.MORGAN, I.G., ROSE, K.A., ALSPAC Study Does Not Support a Role for Vitamin D in the

Prevention of Myopia, *Invest Ophth Vis Sci*, **55**, 2014, 8559. https://doi.org/10.1167/iovs.14-15998.
49.GUGGENHEIM, J.A., WILLIAMS, C., NORTHSTONE K. Does vitamin D mediate the protective effects of time outdoors on myopia? Findings from a prospective birth cohort. *Invest. Ophthalmol. Vis. Sci.*,**55**, 2014, 8550-8558
50.KWON, J.W., CHOI, J.A., LA, T.Y., Epidemiologic Survey Committee of the Korean Ophthalmological Society, Serum 25-hydroxyvitamin D level is associated with myopia in the Korea national health and nutrition examination survey. Medicine (Baltimore*)*, **95**(46), 2016; e5012. doi:10.1097/MD.0000000000005012

Manuscript received: 2.04.2020