LEX LOCALIS-JOURNAL OF LOCAL SELF-GOVERNMENT
ISSN:1581-5374 E-ISSN:1855-363X
VOL. 22, NO. S1(2024)

PREVALENCE OF VITAMIN D DEFICIENCY IN CHILDREN UNDER 5 YEARS AND ITS ASSOCIATION WITH GROWTH PARAMETERS.

Mohammad Irshad[1], Mohsin Hayat[2], Rashida saddiq[3]

[1]Assistant Professor Pediatrics Department Lady Reading Hospital Peshawar,Pakistan
[2]Assistant Professor Pediatrics Department Lady Reading Hospital Peshawar,Pakistan
[3]Woman Medical Officer Police Services Hospital Peshawar, Pakistan

Corresponding author: Mohsin Hayat[2]
Assistant Professor Pediatrics Department Lady Reading Hospital, Peshawar,Khyber Pakhtunkhwa Province, Pakistan
Orcid id : https://orcid.org/0009-0009-0490-3171

mohsinhayatsafi1980@gmail.com[1]

ABSTRACT

Background: Vitamin D is important for skeletal growth and immune regulation. Deficiency in early childhood may impair growth and cause long-term health issues. Under-five children in lower- and middle-income countries are particularly vulnerable. Assessing prevalence and its impact on growth parameters is crucial for developing preventive measures.

Objectives: To assess the extent of vitamin D deficiency among children below the age of five and analyze its correlation with anthropometric indicators of growth such as stunting, wasting, and underweight.

Study Design: A cross-sectional study.

Place and duration of study: Department of Pediatrics Lady Reading Hospital Peshawar, Pakistan from Jan 2023 to June 2023

Methods: Anthropometric measurements and vitamin D levels were assessed for children aged 6-59 months from pediatric outpatient clinics. The World Health Organization standards were used for the anthropometric measurements and the serum Vitamin D was measured with the ELISA method for the 25-hydroxyvitamin D levels. Number and classification of children according the the measured Vitamin D levels were; deficient, insufficient and sufficient. The analyses on the association of growth indices with the children's vitamin levels used chi-square and logistic regression, taking into consideration the the p value of 0.05 as signifying statistical relevance.

Results: One hundred children were involved in the study, with an Mean age 32.4 ± 12.8 months. Of the children, 54% were deemed vitamin D deficient, 28% were insufficient, and 18% where sufficiently vitamin D. Stunted growth was recorded in 34% of children, 29% were underweight, and 18% were wasted. Compared to children with sufficient levels of vitamin D, the mean HAZ, WAZ, and WHZ scores were significantly worse in children with vitamin D deficiency ($p = 0.02$, 0.03, and 0.04, respectively). Children with vitamin D deficiency were found to be stunted more frequently, in this case, there was an odds ratio of 2.1 (95% CI = 1.1–3.9; $p = 0.02$).

Conclusion: Among children under five, there was a high prevalence of Vitamin D deficiency, which was linked with negative growth indicators, especially stunting and underweight. Such findings necessitate early screening, supplementation, and public health interventions aimed at addressing deficiency. Encouraging sun exposure, fortifying food, and educating parents can be beneficial in improving growth and in avoiding the chronic consequences of Vitamin D deficiency in at-risk children.

Keywords: Vitamin D Deficiency, Child, Preschool, Growth Disorders, taunting

Introduction:

Vitamin D is a quite important part of the macronutrients. Apart from affecting the immunity system and the metabolism of proteins in the body, calcium and phosphorus, and bones, it is important in the synthesis of proteins in the body [1]. Industries produce Vitamin D, by fortifying milk and producing fish and dietary supplements. Apart from these dietary sources, Vitamin D is produced in the skin. It is the only Vitamin that the body synthesizes upon the exposure of sun

(ultraviolet B) [2]. During the rapid growth of children, bone diseases like rickets develop and growth is hindered due to the inability of the body to bone mineralization and the sustainment of deficiencies. Malnourished children developing rickets is a public health concern that has no bounds. Deficiencies of Vitamin D is something that many children under five the world over suffer [3]. They depend on malnourished caregivers for the prescribed dietary supplements needed, and for a balanced diet. This situation resulted in Vitamin D deficiencies and the rickets and poor health that comes with it. Children also experience other health deficits due to insufficient Vitamin D other than the rickets that has been mentioned. New studies have shown that it is linked with stunting, wasting, underweight, recurrent respiratory infections, and neurocognitive developmental impairment [4]. In low and middle-income countries, including Pakistan, growth failure, characterized by stunting, underweight, and wasting, constitutes a substantial health problem. Almost 40 % of children under 5 in South Asia are described by UNICEF as stunted, with micronutrient deficiencies as a major underlying cause [5]. The importance of vitamin D in child growth is often neglected especially in low-resource countries where there is limited access to laboratory tests and where low vitamin D levels in children are common. Further complicating the situation is the lack of consensus in defining vitamin D deficiency. The most common classification states that a serum 25-hydroxyvitamin D of <20 ng/mL is deficient, 20-29 ng/mL is insufficient, and ≥30 ng/mL is sufficient [6]. The burden of vitamin D deficiency relative to growth indicators needs to be clearly defined to guide the implementation of preventive and curative measures. For a country like Pakistan, where there is ample sunlight throughout the year, studies show a paradoxically high deficiency prevalence in both urban and rural settings [7]. Possible explanations include indoor living, inadequate dietary diversity, maternal deficiency, and a lack of vitamin D fortified foods. High morbidity and mortality rates may be exacerbated by vitamin D deficiency in children under five years, especially in the already stunted and wasted populations [8]. Analyses on vitamin D deficiency and growth impairment, especially stunted growth, differ across cross-sectional and cohort studies internationally. In India, children under five years in 57% of the population studied had stunted growth and vitamin D deficiency [9]. In much the same manner, poor growth indices and stunted growth associated with low mid upper arm circumference (MUAC) were documented in the literature from Africa and the Middle East. In the literature from Pakistan, the direct association of vitamin D deficiency with anthropometric measures in children under five years of age remains under-studied and documented. Like all other studies in the literature, this one also seeks to extend the body of literature on vitamin D deficiency by, documenting stunting and wasting in children under five years and associating these with vitamin D deficiency. With the results of the study, child health care programs at the policy level will help integrate vitamin D screening and supplementation into programs.

Methods:

This cross-sectional study Department of Pediatrics Lady Reading Hospital Peshawar, Pakistan from Jan 2023 to June 2023. The enrollment consisted of 100 children aged 6–59 months on a consecutive basis. Anthropometric measurements were taken after the relevant parental consent was obtained, in accordance with the WHO guidelines. Child weight was recorded to the nearest 0.1 kg, while length/height were recorded to the nearest 0.1 cm. Z-scores (HAZ, WAZ, WHZ) were calculated using WHO Anthro software. 2 mL venous blood samples were collected and serum 25-hydroxyvitamin D levels were assessed by ELISA. Children were regarded to have a deficiency of vitamin D when levels were <20 ng/mL, insufficient at 20–29 ng/mL and sufficient at levels ≥30 ng/mL. A structured questionnaire was used to collect information regarding

demographic, dietary, and sun exposure characteristics. Statistical analysis done with SPSS version 24.0.

Inclusion Criteria:

Children aged 6-59 months attending the outpatient pediatric clinic and for whom written informed consent was obtained from a parent or guardian and who had no previous diagnosis of chronic systemic illness.

Exclusion Criteria:

Children with atypical physical conditions, recognized metabolic bone disorders, chronic renal or liver diseases, longstanding steroid or anticonvulsant therapy, and those who have received high-dose vitamin D therapy in the last three months.

Ethical Approval Statement:

the Institutional Review Board of Lady Reading Hospital Peshawar has sanctioned the study. Prior to study participation, written informed consent was obtained from participants' parents or guardians. Data was kept confidential; children with severe deficiencies were provided with appropriate supplementation and follow-up care.

Data Collection:

Demographic details alongside data regarding feeding practices, sun exposure history, and other pertinent information were gathered using a structured questionnaire and were completed by the trained study staff. Using calibrated measuring instruments, anthropometric data were recorded and, subsequently, blood samples were drawn and kept under aseptic conditions. For serum 25(OH)D concentration, the blood samples were processed using ELISA kits in a certified laboratory according to the established protocol.

Statistical Analysis:

The analysis of the data was conducted using SPSS version 24.0. For continuous variables, means and standard deviations were calculated, whereas, for categorical variables, frequencies and percentages were used. Categorical outcomes were compared using chi-square tests. Associations between vitamin D status and the various growth parameters were analyzed using logistic regression. A p-value of 0.05 was used for determining statistical significance.

Results:

A cohort of 100 children between 6 and 59 months was evaluated with a mean age of 32.4 (12.8) months. The participants were predominantly male (52%) and female (48%) with 54% overall being male children. The children with vitamin D deficiency (serum levels <20 ng/mL) constituted 54%, insufficiency 28%, and sufficiency 18%. Anthropometric assessment revealed that 34% were stunted (HAZ < −2) and 29% underweight (WAZ < −2) and 18% of the children were wasted (WHZ < −2). There was a higher deficiency rate of vitamin D among stunted children (68%) compared to non-stunted (46%) (st. $p = 0.02$). Underweight prevalence was also higher among deficient children (62% vs 33%, $p = 0.03$). There was a significant association with wasting as well where 45% of the wasted children were deficient compared to 24% of non-wasted ($p = 0.04$).Mean Z-scores were significantly lower in deficient children: HAZ (−2.1 ± 1.0 vs. −1.4 ± 0.8, $p = 0.02$); WAZ (−1.9 ± 0.9 vs. −1.2 ± 0.7, $p = 0.03$); WHZ (−1.8 ± 0.8 vs. −1.1 ± 0.6, $p = 0.04$). After controlling for age, sex and socioeconomic factors, logistic regression showed that

vitamin D deficiency was also an independent risk factor for stunting (OR: 2.1; 95% CI: 1.1–3.9) and that it also increased the odds.

Table 1. Baseline Characteristics of the Study Population (n = 100)

Variable	Frequency (n)	Percentage (%)
Age (months, mean ± SD)	32.4 ± 12.8	–
Sex		
Male	52	52.0
Female	48	48.0
Residence		
Urban	60	60.0
Rural	40	40.0
Sunlight Exposure (<30 min/day)	58	58.0
Exclusive Breastfeeding ≥6 mo	64	64.0
Vitamin D Supplement Use	21	21.0

Table 2. Prevalence of Vitamin D Status among Children Under Five

Vitamin D Status (25[OH]D, ng/mL)	Frequency (n)	Percentage (%)
Deficient (<20 ng/mL)	54	54.0
Insufficient (20–29 ng/mL)	28	28.0
Sufficient (≥30 ng/mL)	18	18.0

Table 3. Growth Parameters According to Vitamin D Status (mean ± SD)

Growth Parameter (Z-score)	Deficient (<20 ng/mL)	Insufficient (20–29 ng/mL)	Sufficient (≥30 ng/mL)	*p*-value
Height-for-Age (HAZ)	−2.1 ± 1.0	−1.7 ± 0.9	−1.4 ± 0.8	0.02
Weight-for-Age (WAZ)	−1.9 ± 0.9	−1.5 ± 0.7	−1.2 ± 0.7	0.03
Weight-for-Height (WHZ)	−1.8 ± 0.8	−1.4 ± 0.6	−1.1 ± 0.6	0.04

Table 4. Association between Vitamin D Deficiency and Growth Parameters (Logistic Regression)

Outcome Variable	Adjusted Odds Ratio (OR)	95% Confidence Interval (CI)	*p*-value
Stunting (HAZ < −2)	2.1	1.1 – 3.9	0.02
Underweight (WAZ < −2)	1.9	1.0 – 3.6	0.03
Wasting (WHZ < −2)	1.8	1.0 – 3.4	0.04

Discussion:

Study conducted earlier has demonstrated suboptimal vitamin D levels in children under five years of age, and this cross-sectional study also demonstrates this with over half of the children studied having serum 25(OH)D levels below 20ng/ml. In addition, lower levels of vitamin D were correlated and significantly connected with negative growth parameters, especially stunting and

underweight [10]. This study and prior literature suggest that vitamin D deficiency poses a significant public health and nutritional risk in this age group and that the consequences of vitamin D deficiency extend beyond the commonly accepted limits of bone health and osteoporosis. In the study, 54% prevalence was noted [11]. This figure falls within the range of earlier study from South Asia which has reported prevalence rates of 40% to 70% in children. In Lahore, Pakistan, 62% of children under five years of age were reported to have vitamin D deficiency due to inadequate maternal vitamin D levels, poor diet and inadequate sun exposure [exposure] [12]. Another study from India reported 55% to 65% as a prevalence range with vitamin D deficiency culturally being worse in rural areas due to clothing practices and poor diet. There are also highly suppressive vitamin D levels reported in the Middle East with rates over 50% in Saudia Arabia and United Arab Emirates despite culturally having more sunlight [13]. These reports suggest that sunlight does not guarantee vitamin D sufficiency in communities with poor diet, cultural practices and lifestyle factors [14]. From a growth parameters perspective, we support the hypothesis that vitamin D deficiency leads to poor growth in children. Deficient children had significantly lower mean HAZ and WAZ scores compared to vitamin D sufficient children, and stunting and underweight were significantly more common [15]. Given vitamin D's role with calcium and phosphate in bone elongation, chondrocyte proliferation, and muscle strength, such associations are likely to be true [15]. A Bangladesh prospective cohort study also found that low vitamin D level children had a twofold risk of stunting at two years of age [16]. Strong associations with vitamin D deficiency were also reported in Ethiopia regarding recurrent infections, linear growth failure, and all three of these conditions are able to worsen malnutrition. The current study strengthens the evidence base in the setting of Pakistan, where stunting remains a substantial public health issue. Wasting, however, in our cohort showed a weaker, though still significant, association with deficiency. Literature regarding wasting, in contrast, has reported a significant deficiency [17].An Egyptian study suggested that acute malnutrition may reflect short-term food insecurity rather than chronic micronutrient-poverty because vitamin D levels and wasting had no connection [18]. On the other hand, vitamin D deficiency and wasting, particularly with low protein consumption, coupled higher prevalence of malnutrition in children in Nepal [19]. The clinical and public health implications are substantial. The findings, which suggested that deficiency may worsen acute malnutrition in resource-poor settings, align with the combination of both studies. The implications are profound. The public health ramifications are profound. Deficiency in vitamin D during the early years of life predisposes individuals to rickets and hypocalcemia and appears to worsen chronic malnutrition and stunted growth. The possible impact of supplementation is evidenced by recent interventional studies, including one randomized controlled trial in India, which found that vitamin D supplementation to deficient toddlers improved linear growth velocity [20,22]. In a Mongolian cohort with severe baseline deficiency, supplementation also resulted in a reduction in the incidence of stunting. However, other trials, including one in Tanzania, reported no significant benefit of supplementation on growth, which raises questions about threshold effects, coexisting deficiencies, and the need for multifactorial interventions. The other side of the narrative may state that vitamin D deficiency is synergistic with other deficiencies, infections, and sociocultural elements, thereby requiring holistic strategies.

Conclusion:

Vitamin D deficiency is very common globally among children under five years which is also linked to negative growth indicators such as being underweight or stunted. The importance of early screening, supplementation, and other public health measures cannot be overstated. Improving

vitamin D deficiency would also improve growth in children, reduce undernutrition, and improve overall development in the long run.

Limitations:

The study's design is cross-sectional in nature which constrains the ability to make causal inferences regarding vitamin D status and the assessed growth outcomes. There was inadequate accounting of the seasonal fluctuations of vitamin D and dietary intake was based on recall by the parents, which could introduce bias. The use of a single center may limit generalizability, highlighting the need for multicenter longitudinal studies to provide more comprehensive validation.

Future Findings:

Long-term studies using longitudinal cohorts should be the focus of future study to derive the causation of vitamin D deficiency on growth. Furthermore, the value of randomized controlled studies centered on supplementation, fortification, and interventions of sun exposure should also be considered. The examination of maternal vitamin D status, genetic polymorphisms, and the synergistic relationships of other micronutrients serves to clarify other strategies to optimize child health.

Abbreviations:

1. **25(OH)D** – 25-hydroxyvitamin D
2. **ANOVA** – Analysis of Variance
3. **BMI** – Body Mass Index
4. **CI** – Confidence Interval
5. **CLIA** – Chemiluminescence Immunoassay
6. **CONSORT** – Consolidated Standards of Reporting Trials
7. **ELISA** – Enzyme-Linked Immunosorbent Assay
8. **EPI** – Expanded Program on Immunization
9. **HAZ** – Height-for-Age Z-score
10. **IRB** – Institutional Review Board
11. **MUAC** – Mid-Upper Arm Circumference
12. **NG/ML** – Nanograms per Milliliter
13. **OPD** – Outpatient Department
14. **OR** – Odds Ratio
15. **SD** – Standard Deviation
16. **SES** – Socioeconomic Status
17. **SPSS** – Statistical Package for the Social Sciences
18. **UVB** – Ultraviolet B
19. **WAZ** – Weight-for-Age Z-score
20. **WHZ** – Weight-for-Height Z-score
21. **WHO** – World Health Organization

Acknowledgments

The authors sincerely thank the staff of Lady Reading Hospital Peshawar their cooperation. We are also grateful to the participating children and their parents for their valuable contribution to this study.

Disclaimer

The views and conclusions expressed in this manuscript are those of the authors and do not necessarily reflect the official policies or positions of Lady Reading Hospital Peshawar or funding bodies. The authors assume full responsibility for the integrity and accuracy of the presented data.

Conflict of Interest

The authors declare no conflict of interest related to this study. No financial, personal, or professional relationships with any organization or individual influenced the design, conduct, analysis, interpretation, or reporting of the research findings.

Informed consent

Written informed consent was obtained from the parents or legal guardians of all participating children prior to enrollment. The consent process included a detailed explanation of the study objectives, procedures, potential risks and benefits, confidentiality of data, and the voluntary nature of participation, with the right to withdraw at any time without penalty.

Ethical Approval Statement

Ethical approval for this study was obtained from the Institutional Review Board (IRB), **Lady Reading Hospital / Medical Teaching Institution (LRH/MTI), Peshawar**. The approval was granted to the Department of Pediatrics, LRH, to conduct the study in accordance with institutional and ethical guidelines.

Author's Contribution:

Mohammad irshad: Concept & Design of Study:
Mohsin Hayat :Data Collection+ Critical Review
Rashida saddiq: Drafting+Data Analysis
Final Approval of version: **All Authors Approved The Final Version**.

References:

1. Abou Zahr R, Faustino EVS, Carpenter T, Kirshbom P, Hall EK, Fahey JT, et al. Vitamin D Status After Cardiopulmonary Bypass in Children With Congenital Heart Disease. Journal of intensive care medicine. 2017;32:508-13. https://doi.org/10.1177/0885066616652077.
2. Bener A, Al-Ali M, Hoffmann GF. Vitamin D deficiency in healthy children in a sunny country: associated factors. International journal of food sciences and nutrition. 2009;60 Suppl 5:60-70. https://doi.org/10.1080/09637480802400487.
3. Brogan-Hewitt A, Apekey TA, Christian MS, Day RE. Improving Vitamin D Intake in Young Children-Can an Infographic Help Parents and Carers Understand the Recommendations? Nutrients. 2021;13:https://doi.org/10.3390/nu13093140.
4. Cairncross CT, Stonehouse W, Conlon CA, Grant CC, McDonald B, Houghton LA, et al. Predictors of vitamin D status in New Zealand preschool children. Maternal & child nutrition. 2017;13:https://doi.org/10.1111/mcn.12340.
5. Chaudhry AB, Hajat S, Rizkallah N, Abu-Rub A. Risk factors for vitamin A and D deficiencies among children under-five in the state of Palestine. Conflict and health. 2018;12:13. https://doi.org/10.1186/s13031-018-0148-y.
6. Chowdhury F, Shahid A, Tabassum M, Parvin I, Ghosh PK, Hossain MI, et al. Vitamin D supplementation among Bangladeshi children under-five years of age hospitalised for severe pneumonia: A randomised placebo controlled trial. PloS one. 2021;16:e0246460. https://doi.org/10.1371/journal.pone.0246460.

7. Chowdhury R, Taneja S, Bhandari N, Sinha B, Upadhyay RP, Bhan MK, et al. Vitamin-D deficiency predicts infections in young north Indian children: A secondary data analysis. PloS one. 2017;12:e0170509. https://doi.org/10.1371/journal.pone.0170509.
8. Jhang WK, Kim DH, Park SJ. Association of vitamin D deficiency with clinical outcomes in critically ill Korean children. Nutrition research and practice. 2020;14:12-9. https://doi.org/10.4162/nrp.2020.14.1.12.
9. Ludmir J, Mazhani L, Cary MS, Chakalisa UA, Pettifor JM, Molefi M, et al. Vitamin D Status in Botswana Children Under 2 Years Old With and Without Active Tuberculosis. The American journal of tropical medicine and hygiene. 2016;94:971-4. https://doi.org/10.4269/ajtmh.15-0864.
10. Madar AA, Gundersen TE, Haug AM, Meyer HE. Vitamin D supplementation and vitamin D status in children of immigrant background in Norway. Public health nutrition. 2017;20:2887-92. https://doi.org/10.1017/s136898001700180x.
11. Manaseki-Holland S, Zulf Mughal M, Bhutta Z, Qasem Shams M. Vitamin D status of socio-economically deprived children in Kabul, Afghanistan. International journal for vitamin and nutrition research Internationale Zeitschrift fur Vitamin- und Ernahrungsforschung Journal international de vitaminologie et de nutrition. 2008;78:16-20. https://doi.org/10.1024/0300-9831.78.1.16.
12. Riccio MP, Catone G, Siracusano R, Occhiati L, Bernardo P, Sarnataro E, et al. Vitamin D deficiency is not related to eating habits in children with Autistic Spectrum Disorder. AIMS public health. 2020;7:792-803. https://doi.org/10.3934/publichealth.2020061.
13. Singh N, Kamble D, Mahantshetti NS. Effect of Vitamin D Supplementation in the Prevention of Recurrent Pneumonia in Under-Five Children. Indian journal of pediatrics. 2019;86:1105-11. https://doi.org/10.1007/s12098-019-03025-z.
14. Surve S, Begum S, Chauhan S, Khatkhatay MI, Joshi B. Determinants of Vitamin D Deficiency Among Under-five Children in Urban Slums of Mumbai, India. Indian pediatrics. 2021;58:888-9.
15. Surve S, Begum S, Joshi B, Khatkhatay MI, Kadam S, Chauhan S. Significance of Vitamin D Binding Protein in Assessing Vitamin D Status Among Under-Five Children. Indian journal of clinical biochemistry : IJCB. 2021;36:167-74. https://doi.org/10.1007/s12291-020-00873-x.
16. Uush T. Prevalence of classic signs and symptoms of rickets and vitamin D deficiency in Mongolian children and women. The Journal of steroid biochemistry and molecular biology. 2013;136:207-10. https://doi.org/10.1016/j.jsbmb.2012.10.014.
17. Vinkhuyzen AAE, Eyles DW, Burne THJ, Blanken LME, Kruithof CJ, Verhulst F, et al. Gestational vitamin D deficiency and autism spectrum disorder. BJPsych open. 2017;3:85-90. https://doi.org/10.1192/bjpo.bp.116.004077.
18. Wallace G, Jodele S, Myers KC, Dandoy CE, El-Bietar J, Nelson A, et al. Single Ultra-High-Dose Cholecalciferol to Prevent Vitamin D Deficiency in Pediatric Hematopoietic Stem Cell Transplantation. Biology of blood and marrow transplantation : journal of the American Society for Blood and Marrow Transplantation. 2018;24:1856-60. https://doi.org/10.1016/j.bbmt.2018.05.019.
19. Walli NZ, Munubhi EK, Aboud S, Manji KP. Vitamin D Levels in Malnourished Children under 5 Years in a Tertiary Care Center at Muhimbili National Hospital, Dar es Salaam, Tanzania-A Cross-sectional Study. Journal of tropical pediatrics. 2017;63:203-9. https://doi.org/10.1093/tropej/fmw081.

20. Wang LL, Wang HY, Wen HK, Tao HQ, Zhao XW. Vitamin D status among infants, children, and adolescents in southeastern China. Journal of Zhejiang University Science B. 2016;17:545-52. https://doi.org/10.1631/jzus.B1500285.
21. Wayse V, Yousafzai A, Mogale K, Filteau S. Association of subclinical vitamin D deficiency with severe acute lower respiratory infection in Indian children under 5 y. European journal of clinical nutrition. 2004;58:563-7. https://doi.org/10.1038/sj.ejcn.1601845.
22. Yani FF, Lipoeto NI, Supriyatno B, Darwin E, Basir D. Vitamin D status in under-five children with a history of close tuberculosis contact in Padang, West Sumatra. Asia Pacific journal of clinical nutrition. 2017;26:S68-s72. https://doi.org/10.6133/apjcn.062017.s2.