Journal of Neonatal Surgery
ISSN(Online): 2226-0439
Vol. 14, Issue 4s (2025)
https://www.jneonatalsurg.com

OPEN ACCESS

Correlation Between Hepatocyte Growth Factor Levels and Axial Length in Severe Myopic Patients

Aryani Atiyatul Amra[1,2], Rodiah Rahmawaty Lubis[3], Aznan Lelo[4], Lambok Siahaan[5], Kemala Sayuti[6], Delfitri Munir[7], Rosita Juwita Sembiring[8], Mustafa Mahmud Amin[9]

[1]Department of Ophthalmology, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia

[2]Philosophy Doctor In Medicine Program, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia

[3]Ophthalmology Study Program, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia

[4]Department of Pharmacology, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia

[5]Department of Parasitology, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia

[6]Department of Ophthalmology, Faculty of Medicine, Universitas Andalas, Padang, Indonesia

[7]Department of Ear Nose Throat, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia

[8]Department of Clinical Pathology, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia

[9]Department of Psychiatry, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia

***Corresponding Author:**

Email ID: aryaniamra@yahoo.com

.Cite this paper as: Aryani Atiyatul Amra, Rodiah Rahmawaty Lubis, Aznan Lelo, Lambok Siahaan, Kemala Sayuti, Delfitri Munir, Rosita Juwita Sembiring, Mustafa Mahmud Amin, (2025) Correlation Between Hepatocyte Growth Factor Levels and Axial Length in Severe Myopic Patients. *Journal of Neonatal Surgery*, 14 (4s), 400-403.

ABSTRACT

Background: Operative procedures have led to various side effects, including dry eyes, overcorrection, undercorrection, optical aberrations such as glare, ghost images, halos, and infections.

Objective: To analyze changes in plasma levels of hepatocyte growth factors (HGF) levels and their effects on the progression of axial length (AL) in severe myopia.

Method: This is a cross-sectional study that included all patients with severe myopia seeking treatment at USU Hospital.

Results: A total of 30 patients included in this study, with a mean HGF level of 1.17 ± 0.73 ng/mL. The left eye-AL (LE-AL) averaged 26.21 ± 0.14 mm, and the right eye-AL (RE-AL) averaged 26.17 ± 0.14 mm. Significant moderate positive correlations were found between HGF levels and both LE- AL ($r = 0.479$, $p = 0.007$) and RE-AL ($r = 0.414$, $p = 0.023$).

Conclusion: HGF levels are positively correlated with AL in patients with severe myopia. These suggest that HGF may play a role in the pathogenesis of axial elongation and could serve as a potential biomarker for monitoring disease progression in severe myopia.

1. INTRODUCTION

Severe myopia is associated with oxidative stress, which can contribute to its progression and lead to complications such as uncorrectable visual impairment, potentially resulting in blindness. The primary approaches to managing severe myopia include both conservative and surgical methods. Conservative treatments involve refractive correction, such as wearing glasses or contact lenses, and the use of atropine eye drops. However, surgical procedures have been linked to several side effects, including dry eyes, overcorrection, undercorrection, and optical aberrations such as glare, ghost images, halos, and infections. Similarly, refractive correction methods like glasses and contact lenses also present challenges. Non-compliance with wearing glasses can lead to conditions such as lazy eye (amblyopia), while contact lens use may cause side effects such as infection, inflammation, toxicity, mechanical issues, and dry eyes. (Widodo, 2007; Murray, 2009; Tideman, 2016; AAO, 2019; Ma, 2021).

The prevalence and incidence of myopia, including severe myopia, have increased drastically over the past 20 years and are expected to continue rising significantly until 2050. In 2000, approximately 22.9% of the global population, or 1.4 billion people, had myopia. This figure increased to 27% (1.9 billion people) in 2010 and further rose to 33% (2.5 billion people) in

2020. By 2050, it is projected that myopia will affect up to 52% of the global population, reaching an estimated 4.9 billion people. (Zhu, 2012; Czepita, 2014; Holden, 2016).

In line with the increasing prevalence of myopia, there has also been a rise in the severity of the condition, particularly in cases of high myopia. Severe myopia has been reported as the seventh leading cause of blindness in the United States, the fourth in Hong Kong, and the second in China and Japan. Globally, the prevalence of high myopia was 2.9% (224 million people) in 2010 and is projected to reach 10% of the world's population, approximately 925 million people, by 2050. (WHO, 2017; Grzybowski, 2020).

According to the 2013 Basic Health Research Report, the prevalence of refractive disorders in Indonesia was 4.6%, while in North Sumatra, it was 4.0%. A study by the Ministry of Health of the Republic of Indonesia found that the prevalence of uncorrected refractive disorders in Sumatra was 12.9% (Riskesdas, 2013; Mahayana, 2017).

The rapid increase in myopia prevalence, combined with its vision-threatening complications, represents a significant public health burden. Studies examining the relationship between myopia and ocular pathology have reported distinct differences between mild-to-moderate and severe myopia. In severe myopia, hypoxia leads to increased oxidative stress, which triggers continuous axial elongation of the eyeball, resulting in functional damage. This process causes thinning of the sclera as well as atrophy of the retinal pigment epithelium and choroid. A logical assumption is that greater axial length is associated with a higher risk of visual impairment. Currently, severe myopia is one of the leading causes of blindness worldwide, often linked to disease progression conditions such as glaucoma, cataracts, retinal detachment, and myopic macular degeneration (Tideman, 2016; Merida, 2020).

Axial length is a crucial factor in refractive disorders such as myopia and hypermetropia. It is defined as the distance from the cornea's anterior surface to the retinal pigment epithelium and is commonly measured using ultrasonography. During early childhood, the eyeball undergoes significant growth. At birth, the axial length typically ranges from 16.6 mm to 16.8 mm, with the visual system still underdeveloped until around age three. Between birth and six years, the axial length increases by approximately 5 mm, usually leading to emmetropia rather than myopia.

Axial length development occurs in three phases, rapid growth phase (birth – 18 months),

infantile phase (2–5 years), and juvenile phase (5–13 years). This structured growth pattern explains how the eye adapts during development, ensuring proper visual function. (Meng, 2011; AAO, 2019; Bach, 2019).

Another important aspect of severe myopia management is environmental and dietary modification. Severe myopia linked to oxidative stress is more common in cases with poor disease progression. Antioxidants play a crucial role in neutralizing free radicals, preventing oxidative stress-related damage, and maintaining cellular health (Widodo, 2007; Murray, 2009; Audrey, 2012; Gong, 2017; AAO, 2019; Wu, 2019).

Various biological substances have been explored as biomarkers of oxidative stress. Oxidative stress also arises from reduced oxygen and nutrient availability, leading to ischemic and microvascular damage. Excess free radical production from lipid and protein metabolism, combined with inadequate antioxidant intake, exacerbates oxidative damage. Micronutrients found in plants, such as vitamins A, C, and E, folic acid, carotenoids, anthocyanins, and polyphenols, play a crucial role in neutralizing free radicals (Gill, 2002; Murray, 209).

Hepatocyte growth factor (HGF) is a cytokine found in various ocular tissues, including the RPE, cornea, and choroidal endothelial cells. HGF promotes endothelial development and neovascularization via the c- MET signaling pathway. Under hypoxic conditions, HGF enhances retinal vascular permeability and increases eNOS activity via the phosphoinositide 3-kinase/Akt pathway, leading to microvascular vasodilation. In myopia, HGF has been linked to increased matrix metalloproteinase 2 (MMP-2) expression in scleral fibroblasts, which contributes to extracellular matrix degradation and axial elongation. Overexpression of HGF has been reported in severe myopia (Khor, 2010; Merida, 2020).

Despite these findings, no published research has specifically examined changes in HGF levels and their impact on axial elongation in severe myopia.

2. METHODS

This study employed a cross-sectional study design. The research was conducted at USU Hospital and the Integrated Laboratory (Immunology Laboratory) of the Faculty of Medicine, Universitas Sumatera Utara.

The target population included all patients with severe myopia seeking treatment at USU Hospital. The accessible population consisted of patients with severe myopia treated at USU Hospital who met the inclusion criteria.

The sample size calculation was based on the minimum required number of participants for HGF which are 30 participants. To account for potential dropout or loss to follow-up, the sample size was increased by 20%, resulting in a minimum of 30 participants per group (Bhatia, 2006; Navea, 2018).

The sampling technique used was non-probability sampling with a consecutive sampling method, where all eligible subjects who met the inclusion criteria were enrolled consecutively until the required sample size was reached.

3. RESULTS

A total of 30 patients were included in the study. The demographic and clinical characteristics of the patients are summarized in Table 1. Table 2 presents the correlation between HGF levels and AL in patients with severe myopia. The mean HGF level was 1.17 ± 0.73 ng/mL. The axial length of the left eye (LE-AL) had a mean of 26.21 ± 0.14 mm, while the axial length of the right eye (RE-AL) had a mean of 26.17 ± 0.14 mm. A statistically significant moderate positive correlation was observed between HGF levels and LE-AL (r = 0.479, p = 0.007). Similarly, a statistically significant moderate positive correlation was found between HGF levels and RE-AL (r = 0.414, p = 0.023).

Table 2. Correlation Between HGF and Axial Length Among Patients With Severe Myopia

Parameter	Mean ± SD	Coefficient Correlation	P value
HGF (ng/mL)	1.17 ± 0.73		
LE – AL (mm)	26.21 ± 0.14	0.479	0.007*
RE – AL (mm)	26.17 ± 0.14	0.414	0.023*

HGF, hepatocyte growth factor; AL, axial length, LE, left eye; RE, right eye

**Spearman correlation coefficient*

REFERENCES

[1] American Optometric Association. 2015. Optometric Clinical Practice Guideline: Care of the Patient with Myopia.

[2] Bach, A., Villegas, VM, Gold, US, Shi, W. and Murray, TG, 2019. Axial length development in children *International journal of ophthalmology* , *12* (5),:815- 9

[3] Chepita, D., 2014. Myopia: incidence, pathogenesis, management and new possibilities of treatment. *Russ Ophthalmol J* , *7* (1),:96-101.

[4] Gil, MI, Tomás-Barberán, FA, Hess-Pierce, B. and Kader, AA, 2002. Antioxidant capacities, phenolic compounds, carotenoids, and vitamin C contents of nectarines, peach, and plum cultivars from California. *Journal of agriculture and food chemistry* , *50* (17), :4976- 82.

[5] Grzybowski, A., Kanclerz, P., Tsubota, K., Lanca, C. and Saw, S.M., 2020. A review on the epidemiology of myopia in school children worldwide. *BMC ophthalmology* , *20* (1):1-11.

[6] Holden, BA, Fricke, TR, Wilson, DA, Jong, M., Naidoo, KS, Sankaridurg, P., Wong, TY, Naduvilath, TJ and Resnikoff, S., 2016. Global prevalence of myopia and high myopia and temporal trends from 2000 through 2050. *Ophthalmology* , *123* (5), :1036-42.

[7] Khor, C.C., Grignani, R., Ng, DP, Toh, KY, Chia, K.S., Tan, D., Goh, D.L. and Saw, SM, 2009. cMET and refractive error progression in children. *Ophthalmology* , *116* (8), :1469-74.

[8] Khor, CC, Fan, Q., Goh, LK, Wong, TY, Li, YJ, Cheung, N., Seielstad, M., Goh, DL, Young, TL, Tai, ICE and Saw, SM, 2010. Hepatocytes growth factor and retinal arteriolar diameter in Singapore Chinese. *Ophthalmology , 117* (5),: 939-45.

[9] Mahayana, IT, Indrawati, SG, Pawiroranu, S. 2017. The prevalence of uncorrected refractive error in urban, suburban, exurban and rural primary school children in Indonesian population. *Int J Ophthalmol* ;10(11):1771-6

[10] Mérida, S., Villar, V.M., Navea, A., Desco, C., Tello, S.M., Peris, C., *et al* . 2020. Imbalance Between Oxidative Stress and Growth Factors in Human High Myopia. *Front Physiol* ;11(463). doi:10.3389/fphys.2020.00463

[11] Meng, W., Butterworth, J., Malecaze, F., Calva, P. 2011. Axial Length of Myopia: A Review of Current Research. Ophthalmologica;225:127-34. doi: 10.1159/000317072 Murray, RK, Granner, DK, Rodwell, VW 2009. Biochemistry Harper 27 ed.. Jakarta: *Book Medical EGC* .

[12] Tideman, JWL, Snabel, MCC, Tedja, MS, et al. 2016. Association of Axial Length With Risk of Uncorrectable Visual Impairment for European With Myopia. *JAMA Ophthalmol;* 134(12):1355–1363. doi:10.1001/jamaophthalmol.2016.4009

[13] Wang, B., Naid, RK, Qu, X. 2017. Factors related to axial length elongation and myopia progression in orthokeratology practice. *PLoS One*. doi:10.1371/journal.pone.0175913

[14] World Health Organization. 2015. The Impact of Myopia and High Myopia: Report of the joint World Health Organization-Brian Holden Vision Institute Global Scientific Meeting on Myopia. Available from: https://www.who.int/blindness/causes/MyopiaReportforWeb.pdf (Downloaded July 2021) Widodo, Agung, Prillia T. 2007. Pathological Myopia. *Indonesian Journal of Ophthalmology* : 19-26.

[15] Zhu, MM, Yep, MK, Hey, DW, Fun, WY, Ng, PW, Gu, YS, et a. 2012. Investigating the relationship between UMODL1 gene polymorphisms and high myopia: a case–control study in Chinese. *BMC medical genetics* ; *13* (1): 1-10.