

# Pregnancy-induced Progression of Keratoconus in a 37-Year-Old Patient

Juliana Glicéria, Bruno Freitas Valbon, Rodrigo Teixeira Santos, Renato Ambrósio Jr

## ABSTRACT

**Purpose:** To report a case of keratoconus that progressed during pregnancy without any accompanying disease.

**Methods:** A case report.

**Results:** A patient with keratoconus that worsened during pregnancy demonstrates that pregnancy can be a previously unrecognized risk factor for progression of keratoconus.

**Conclusion:** To our knowledge, this is the first case reported in Brazil and the third paper in the world showing pregnancy-induced keratoconus progression in a patient with no accompanying disease.

**Keywords:** Keratoconus, Corneal ectasia, Pregnancy, Risk factors, Case report.

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**Conflict of interest:** None declared

## INTRODUCTION

Keratoconus is characterized by progressive corneal ectasia and estromal thinning, increased myopia and irregular astigmatism.<sup>1</sup> The pathological process underlying keratoconus have not been fully understood, but is accepted that it is a clinical condition with multifactorial etiology that ends in corneal conical protrusion. Many factors can aggravate keratoconus progression such as eye rubbing.<sup>2</sup>

Recently, the effect of pregnancy on the progression of an ectatic condition has been reported. In the literature, four cases of keratoconus progression were reported as developing during pregnancy without any accompanying factors.

This report provides adds to this body of literature with the case of a 37-year-old patient that had stabilized disease for over 10 years.

## CASE REPORT

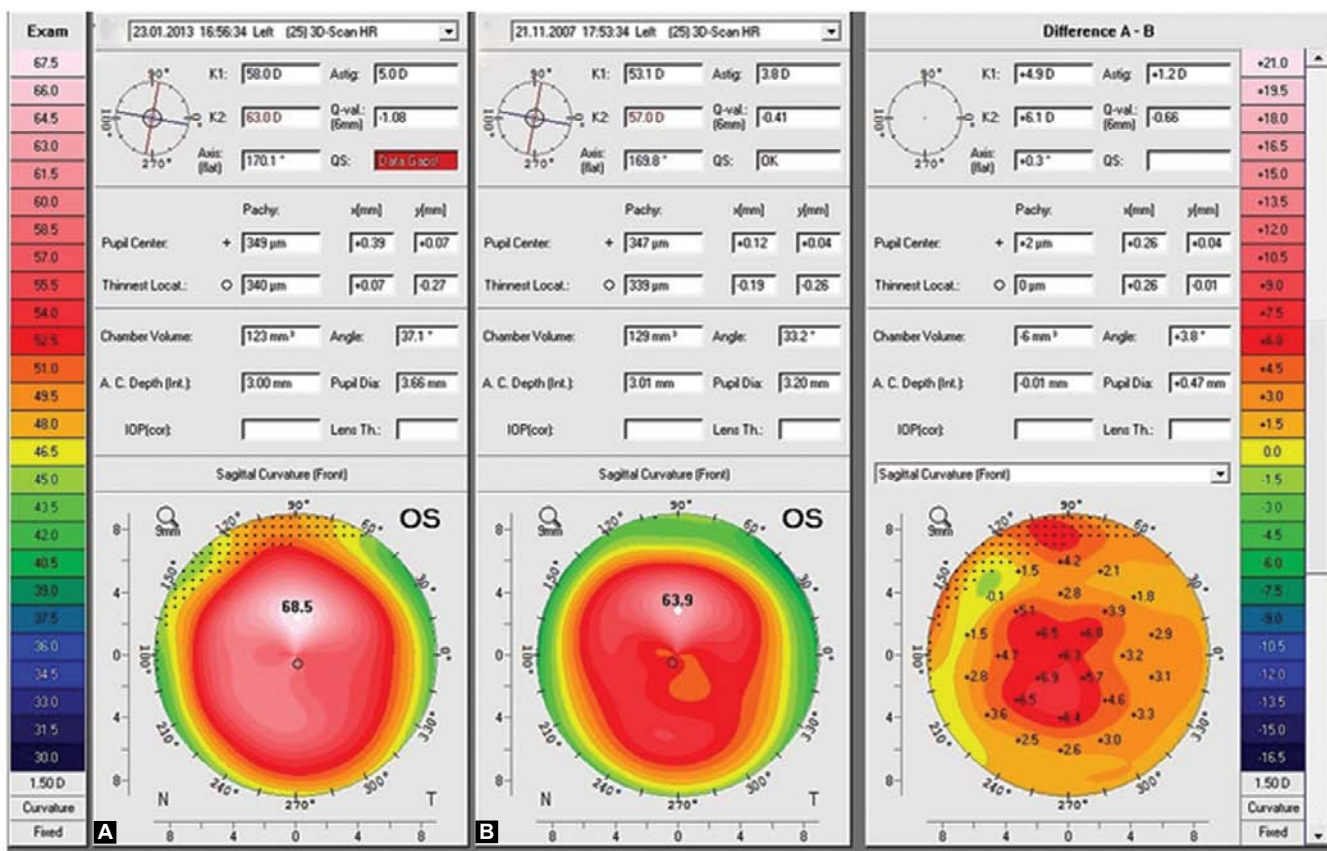
A 37-year-old woman was first seen in the clinic in November 2007 for a second opinion. She had been previously diagnosed as having keratoconus and had presented a relatively stable ectasia in the left eye (OS) for over ten years. She complained of progressive loss of corrected visual acuity during pregnancy that had not improved four after delivery. Her previous medical history consisted of a lamellar keratoplasty in the

right eye (OD) in 2000 and no other comorbidities. There was no family history of keratoconus or corneal transplant, no sporadic eye rubbing, and no known atopic diseases in the patient or her family.

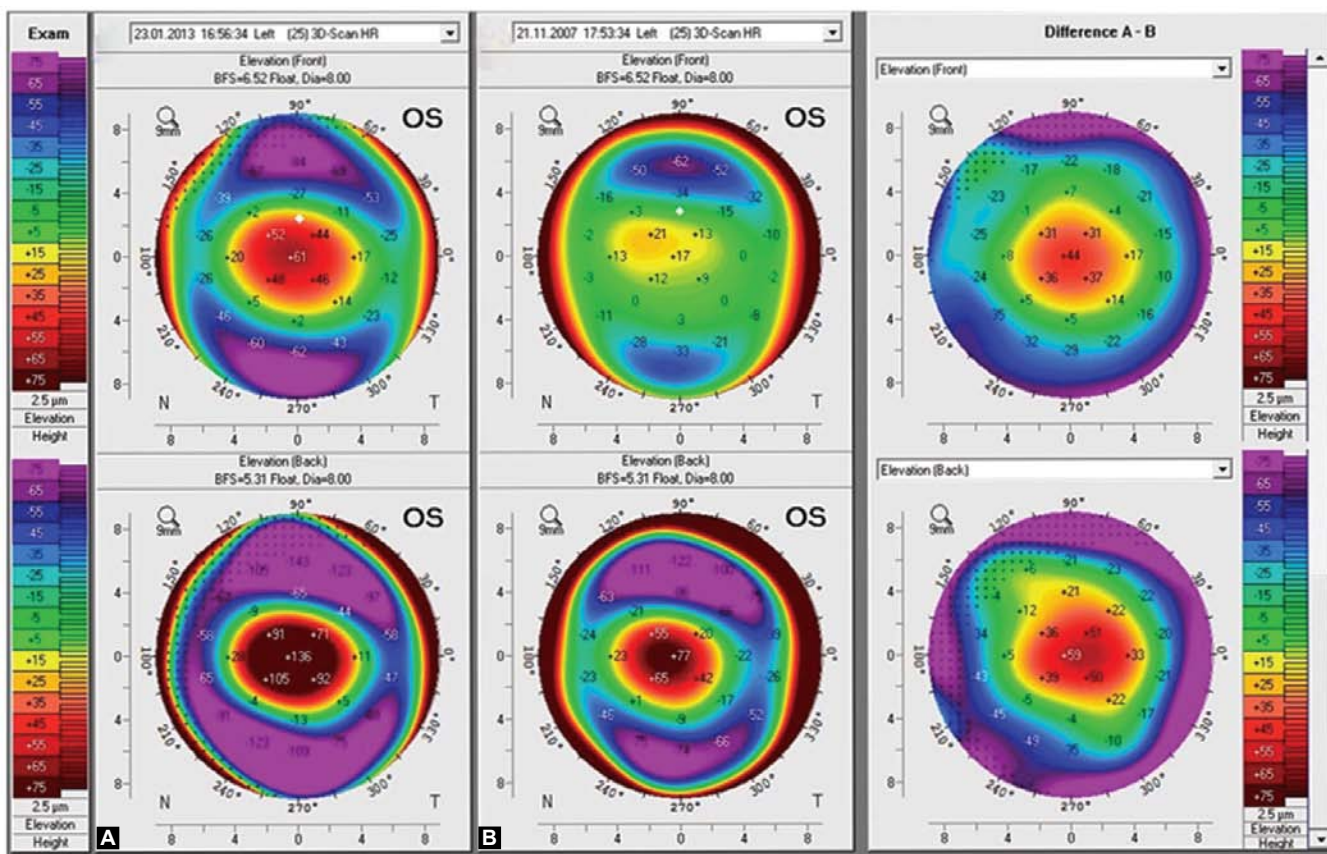
In November 2007, her best corrected visual acuity was 20/30 in the both eyes with her current spectacles. The biomicroscopic examination showed a clear corneal transplant in OD and a transparent cornea in OS with thickened nerves and few papillae. ORA (Ocular Response Analyser) showed a Goldmann correlated intraocular pressure (IOPg) of 2.5 mm Hg, a corneal compensated intraocular pressure (IOPcc) of 8.4 mm Hg, a corneal hysteresis (CH) of 7.1 and a corneal resistance factor (CRF) of 3.7 in OS. Corneal topography measured by front sagittal curvature in Pentacam (Oculus Optikgeräte GmbH, Wetzlar, Germany) revealed a maximum keratometric power of 63.9 D. The thickness at the thinnest point evaluated was 339  $\mu$ m in the left eye. We observed from the anterior corneal sagittal curvature map a simulated keratometry of 53.1  $\times$  57.0 @169.8 (Figs 1A and B).

In January 2013, the patient returned complaining of worse vision in OS. Best corrected visual acuity was 20/30 in OD and 20/40 in OS. The biomicroscopic examination showed no significant changes. ORA showed an IOPg of 1.7 mm Hg, IOPcc of 9.0 mm Hg, CH of 5.9 and CRF of 2.4, indicating a weaker cornea in OS. We repeated the tomography examination using the Pentacam which showed a maximum keratometric power of 68.5 D and a thinnest point of 340  $\mu$ m in OS. At the anterior corneal sagittal curvature map, we could see an increase in simulated keratometry to 58.0  $\times$  63.0 @ 170.1 D (Figs 1A and B). In front and back elevation maps, we can observe the worsening in corneal protrusion when the maps are compared (Figs 2A and B). These data indicate the deteriorating state of keratoconus in OS.

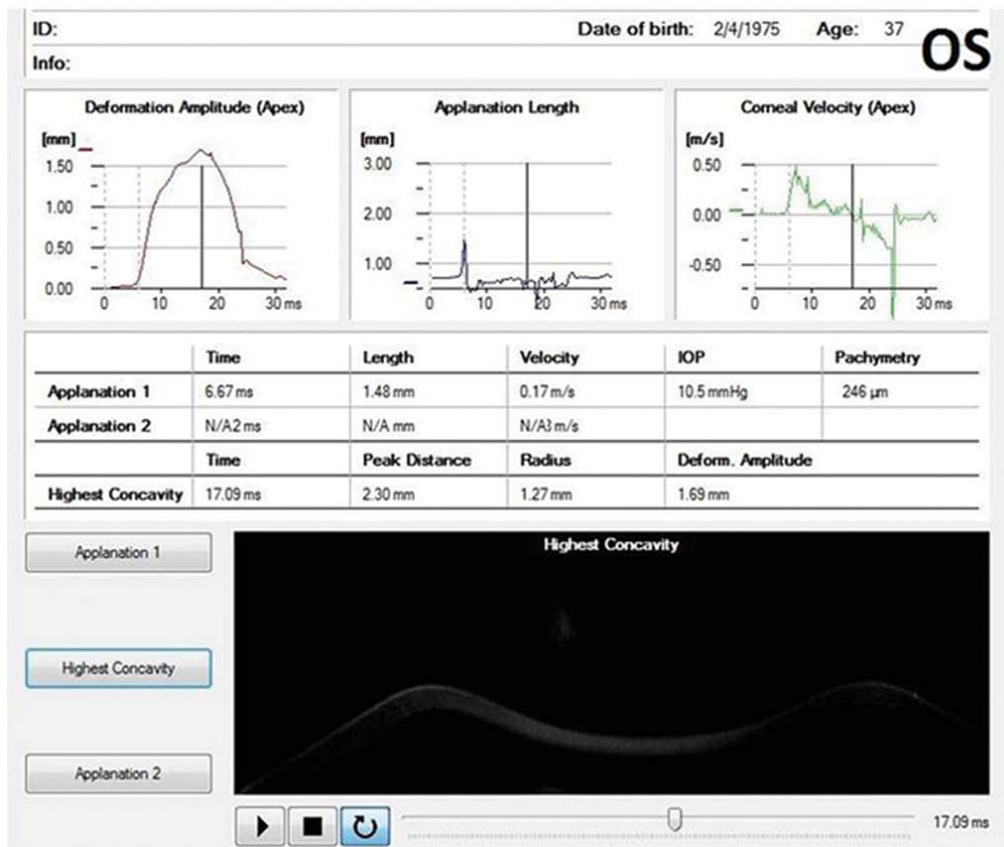
The Corvis ST (Scheimpflug Technology recently introduced by Oculus Optikgeräte GmbH, Wetzlar, Germany) demonstrated a deformation's amplitude of 1.69 mm (Fig. 3). Ambrosio et al<sup>3</sup> reported observed differences in the combined parameters based on a linear regression analysis of data from the Corvis ST for four study groups (i.e. normal, forme frustre keratoconus, asymmetric bow tie, and keratoconus). The mean deformation amplitude was 1.02  $\pm$  0.09 mm (i.e. the range was: 0.78 to 1.26) in the normal eyes reviewed in this article.



**Figs 1A and B:** Evaluation of corneal topographical (front sagittal curvatures maps): after pregnancy (A) and before pregnancy (B) and the differential map. Pentacam (Oculus Optikgeräte GmbH, Wetzlar, Germany)



**Figs 2A and B:** Evaluation of corneal elevation (front and back elevation maps): after pregnancy (A) and before pregnancy (B) and the differential map. Pentacam (Oculus Optikgeräte GmbH, Wetzlar, Germany)



**Fig. 3:** Corneal biomechanical evaluation: increased deformation amplitude index (1.69 mm) demonstrates the cornea's weakness in keratoconus. Corvis (Oculus Optikgeräte GmbH, Wetzlar, Germany)

Considering the treatments available, kerating and corneal cross-linking were recommended to this patient to regularize and strengthen the cornea.

## DISCUSSION

In this case, the patient fulfilled two of the criteria that attest to the progression of keratoconus: an increase in one or more diopters in the mean keratometry and an increase of at least 1.0 diopter in astigmatism or an increase of at least 0.5 diopter in manifest spherical equivalent refraction,<sup>2</sup> confirming that keratoconus was worsening and that precocious intervention was necessary.

In 2010, the Collaborative Longitudinal Evaluation of Keratoconus Study reported the influence of hormone status on the severity and progression of keratoconus involving patients between 48 and 59 years old to evaluate the effects of menopause and use of external hormonal replacement therapy.<sup>4</sup> That study could not detect any influence of hormone status on keratoconus patients. However, they did not include any pregnant patients in that study. The group admitted that the slow progression of keratoconus in that particular age group studied represented a limitation.

Gatzioufas and Thanos<sup>5</sup> have reported a case of hypothyroxinemia-induced acute corneal hydrops during

pregnancy. The authors suggested that the progression was related to thyroid gland dysfunction because the deterioration of keratoconus coincided with the lowest plasma thyroxin level. Hafezi and Iseli<sup>6</sup> reported a case of bilateral iatrogenic keratectasia 26 months after LASIK, which developed during pregnancy.

Our patient, contrary to previous studies, had no associated disease or predisposing factor. Similar to our case, Bilgihan et al<sup>1</sup> reported four cases of keratoconus without any accompanying disease that progressed during pregnancy.

Recent studies have suggested that changes in estrogen levels may play a role in corneal ectasia.<sup>7,8</sup> Estrogen receptors have been identified in cornea,<sup>9-11</sup> and a significant stiffness-reducing effect of estrogen on cornea has been shown in an experimental study. These findings suggest that high estrogen- states, like pregnancy, may predispose biomechanically weak corneas to ectasia development or progression.<sup>12</sup>

Various studies have demonstrated elevated levels of collagenolytic and gelatinolytic activities in keratoconic corneas.<sup>13-17</sup> Matrix metalloproteinase (MMP) levels are increased, whereas tissue inhibitors of MMPs (TIMPs) are decreased in the keratoconic corneas<sup>17-19</sup> as well as during pregnancy too.<sup>20-23</sup> It has been suggested that proteinases



(collagenases and MMPs) may play an important role in the pathogenesis of keratoconus.<sup>24</sup> Furthermore, proteinase enzymes play key roles in various points of pregnancy. These enzymes contribute to the extracellular matrix remodeling required for follicular development and ovulation, for loosening of the collagen framework of the endometrium for implantation, growth and softening of the cervix, and for relaxation of the pelvic bones for delivery.<sup>25-28</sup>

It therefore seems clear that increased levels of proteolytic enzymes and decreased levels of their inhibitors during pregnancy are important for the progression of keratoconus.

An important molecule that plays key roles in pregnancy is relaxin. Relaxin was discovered in 1926 by Hisaw,<sup>29</sup> who noted relaxation of the pubic ligament in virgin guinea pigs after injection of serum from pregnant guinea pigs. The most consistent biological effect of relaxin is its ability to stimulate the breakdown of collagen. It increases the synthesis of the collagen-degrading enzymes and MMPs and decreases the synthesis of TIMPs.<sup>30</sup> Therefore; relaxin may also play a role in the progression of keratoconus during pregnancy through MMPs and TIMPs.

Hormonal changes during pregnancy may affect corneal biomechanics negatively. They are associated with increased corneal thickness, decreased corneal hysteresis and decreased corneal resistant factor. Therefore, pregnancy can be a previously unrecognized risk factor for progression of keratoconus.

If further studies demonstrate a significant risk of keratoconus progression during pregnancy, then corneal cross-linking should be more extensively applied in patients with keratoconus that are considering becoming pregnant. Thus, more studies are required to elucidate the clinical correlation of keratoconus and pregnancy.

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Biomechanics Study Group – Rio de Janeiro, RJ, Brazil, Phone: 552125971132, e-mail: [jugli@globo.com](mailto:jugli@globo.com)

### **Bruno Freitas Valbon**

Postgraduate Student, Department of Ophthalmology, University of São Paulo, São Paulo, Brazil

### **Rodrigo Teixeira Santos**

Fellow, Department of Ophthalmology, Federal University of São Paulo, São Paulo, Brazil

### **Renato Ambrósio Jr**

Founder and Director, Rio de Janeiro Corneal, Tomography and Biomechanics Study Group; Director of Refractive Surgery of Inst. Olhos R Ambrosio and VisareRIO, Rio de Janeiro, RJ, Brazil; Associate Professor, Department of Ophthalmology, Federal University of São Paulo, São Paulo, Brazil

## **ABOUT THE AUTHORS**

### **Juliana Glicéria (Corresponding Author)**

Resident, Department of Ophthalmology, Hospital da Piedade (RJ); Research Associate, Rio de Janeiro Corneal Tomography and