

# The Holmes-Adie Syndrome in the Mona Lisa of Leonardo da Vinci (1452-1519)

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**Abstract.** The literature describes that the renowned artwork of the genius of human anatomy, Leonardo da Vinci (1452-1519), known as Mona Lisa (1503-1506), is among one of the most enigmatic artworks in the History of Art. In this context, many details inserted on the composition of this artwork, including those related to Mona Lisa physical aspects' (anatomy) are controversial. The few known descriptions that provide some thorough indications about the woman who served as the model for this work, were written by Giorgio Vasari (1511-1574) in 1550. According to Vasari, the Mona Lisa is a portrait of Lisa del Giocondo (1479-1542) and although he has given a detailed description concerning Lisa's physical characteristics, some are not fully understood so far. In this context, the unequal size of her pupils stands out, a clinical condition known as anisocoria. On this detail, this Letter presents unprecedented pieces of evidence that the anisocoria represented in Mona Lisa may be an indicator that Lisa del Giocondo had a neurological disorder known as Holmes-Adie Syndrome, which could have been caused by an endocrine disruption of the thyroid hormones. Thus, the pieces of information presented on this Letter are essential for further studies once, through them, it is possible to know more about the physical characteristics and also about the probable health condition of the renowned character of one of the most famous artworks of history. ([www.actabiomedica.it](http://www.actabiomedica.it)).

**Key words:** Leonardo da Vinci, Mona Lisa, Holmes-Adie Syndrome, Thyroid

The literature has described that the renowned artwork of the great Renaissance artist and genius of human anatomy, Leonardo da Vinci (1452-1519), known as *Mona Lisa* or *La Gioconda* (circa 1503-1506), is a portrait of Lisa del Giocondo (1479-1542) [*member of the Gherardini family from the Florentine region and Tuscany – Italy*] (1). Furthermore, the specialized literature also demonstrates that *Mona Lisa's* right eye is most directly facing the source of the light, that comes from her right (1), in doing so, her pupil should be smaller due to the photomotor reflex or pupillary light reflex through the postganglionic supply (oculo-

motor nerve) that promotes the pupil constriction (2). However, the right eye pupil is the bigger one (dilated), in other words, it is not responding to the photomotor reflex (Figure 1). Clinically, this condition may be compatible with a neurological disorder known as Holmes-Adie Syndrome (HAS) (3).

Although there isn't much information in the literature regarding Lisa del Giocondo's health condition at the time Leonardo da Vinci portrayed her, it is still possible to notice some physical characteristics in the portrait of *Mona Lisa* that could provide a probable explanation for the emergence of HAS. See below:

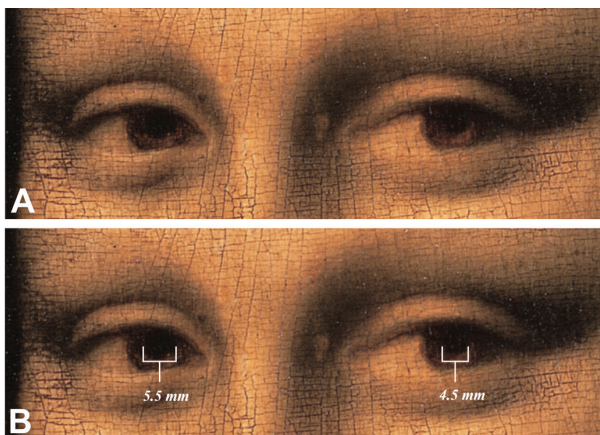
Although he has portrayed Lisa with a veil covering her head, it is still possible to notice that Lisa's hair is thin and not bulky. Moreover, on the Mona Lisa's portrait, Lisa is represented almost without eyebrows/eyelashes (1, 4). Giorgio Vasari (1511–1574) himself describes that Leonardo represented the eyebrows (...) here more close and here more scanty (...); in other words, with sparse areas of brows and lashes around the eyes (almost nonexistent) (1, 4) (Figure 1). Given these facts, it becomes evident the hair scarcity on Lisa's portrait, which could presumably be due to an endocrine disruption of the thyroid hormones known as hypothyroidism, which may provoke hair loss (eyebrows/eyelashes) (5). This would be in perfect accordance with a study (6) published in 2018, where the authors list several reasons to believe that Lisa del Giocondo had hypothyroidism. See some of the reasons described (6) by the authors: 1- Thyroid swellings in the art of the Italian Renaissance were very common and were the most prevalent pathological condition shown in Byzantine artworks. 2- The second important evidence is the fact that she had given birth to her male child, Andrea, recently within months before sitting for the painting. 3- It is possible that she suffered from a subclinical presentation of peripartum thyroiditis, with an early manifestation of hyperthyroidism eventually setting into a chronic phase of hypothyroidism. This, coupled

with the living conditions and iodine-deficient diet of this period in the Florentine region, would have characteristically led to the secondary manifestations of underlying hypothyroidism.

Therefore, it becomes evident that there are many indications that Lisa del Giocondo could have hypothyroidism by the time she was portrayed by Leonardo da Vinci and it is from this context that she may have developed HAS. This hypothesis is mainly due to the fact that although the etiology of HAS is not yet fully known, the association of this syndrome with other disorders has already been described in the literature, particularly with vitamin deficiencies and hypothyroidism (3). Thus, we believe that Lisa del Giocondo may have developed HAS from of a hypothyroidism related illness that could have been the result of a peripartum thyroiditis accentuated by the living conditions of the Florentine region and Tuscany (vitamin/iodine-deficient diet). However, we should also admit that our unifying hypothesis (about HAS in Lisa del Giocondo) may be as plausible as the multiple explanations provided, each open to individual and collective bias.

*“The eye, which is called the window of the soul, is the chief organ whereby the understanding may have the most complete and magnificent view of the infinite work of nature.”*

*Leonardo da Vinci (Vinci 1452 - Amboise 1519)*



**Figure 1.** (A) Detail that emphasizes the eyes of *Mona Lisa* (circa 1503-1506) by Leonardo da Vinci. (B) Observe that the diameter of the right eye's pupil is bigger than the left eye's pupil. This may be demonstrated through *Image Pro Plus Software 6.0* (Media Cybernetics, Silver Spring, MD, USA) which precisely measures the diameters of both pupils. To calibrate the *Image Pro Plus Software*, the following commands were used: *Measure/Calibration/Spatial [Dimensions: 77 x 53 cm]* [Louvre Museum (Paris)]. (<https://focus.louvre.fr/en/mona-lisa>).

**Conflicts of interest:** Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

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