1. **Global Retinoblastoma Presentation and Analysis by National Income Level**
   (Presentación y análisis del retinoblastoma global por nivel de ingreso nacional)

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ABSTRACTO: IMPORTANCE: Early diagnosis of retinoblastoma, the most common intraocular cancer, can save both a child's life and vision. However, anecdotal evidence suggests that many children across the world are diagnosed late. To our knowledge, the clinical presentation of retinoblastoma has never been assessed on a global scale. OBJECTIVES: To report the retinoblastoma stage at diagnosis in patients across the world during a single year, to investigate associations between clinical variables and national income level, and to investigate risk factors for advanced disease at diagnosis. DESIGN, SETTING, AND PARTICIPANTS: A total of 278 retinoblastoma treatment centers were recruited from June 2017 through December 2018 to participate in a cross-sectional analysis of treatment-naive patients with retinoblastoma who were diagnosed in 2017. MAIN OUTCOMES AND MEASURES: Age at presentation, proportion of familial history of retinoblastoma, and tumor stage and metastasis. RESULTS: The cohort included 4351 new patients from 153 countries; the median age at diagnosis was 30.5 (interquartile range, 18.3-45.9) months, and 1976 patients (45.4%) were female. Most patients (n = 3685 [84.7%]) were from low- and middle-income countries (LMICs). Globally, the most common indication for referral was leukocoria (n = 2638 [62.8%]), followed by strabismus (n = 429 [10.2%]) and proptosis (n = 309 [7.4%]). Patients from high-income countries (HICs) were diagnosed at a median age of 14.1 months, with 656 of 666 (98.5%) patients having intraocular retinoblastoma and 2 (0.3%) having metastasis. Patients from low-income countries were diagnosed at a median age of 30.5 months, with 256 of 521 (49.1%) having extraocular retinoblastoma and 94 of 498 (18.9%) having metastasis. Lower national income level was associated with older presentation age, higher proportion of locally advanced disease and distant metastasis, and smaller proportion of familial history of retinoblastoma. Advanced disease at diagnosis was more common in LMICs even after adjusting for age (odds ratio for low-income countries vs upper-middle-income countries and HICs, 17.92 [95% CI, 12.94-24.80], and for lower-middle-income countries vs upper-middle-income countries and HICs, 5.74 [95% CI, 4.30-7.68]). CONCLUSIONS AND RELEVANCE: This study is estimated to have included more than half of all new retinoblastoma cases worldwide in 2017. Children from LMICs, where the main global retinoblastoma burden lies, presented at an older age with more advanced disease and demonstrated a smaller proportion of familial history of retinoblastoma, likely because many do not reach a childbearing age. Given that retinoblastoma is curable, these data are concerning and mandate intervention at national and international levels. Further studies are needed to investigate factors, other than age at presentation, that may be associated with advanced disease in LMICs.