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Measuring Toxocariasis Prevalence In Pediatric Asthma Patients Using Serological And Molecular Biology Approaches Brief Review

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Introduction

Toxocariasis, caused by Toxocara cati or T. canis, is a parasitic infection transmitted to humans through ingestion of infective eggs. The larvae migrate to various tissues, particularly affecting the brain, liver, lungs, and eyes **(Gillespie and Pearson, 2003; Muller and Wakelin, 2002; Overgaauw and Nederland, 1997; Malhotra et al., 2003).** This infection is highly prevalent in developing countries, especially in rural areas.

In children, toxocariasis is associated with asthma, pneumonia, and eosinophilia **(Macpherson, 2013).** Misdiagnosis often leads to inappropriate corticosteroid treatment, worsening their condition **(Overgaauw and Nederland, 1997).** Environmental exposure to Toxocara may increases asthma risk or exacerbate pulmonary symptoms in asthmatic patients **(Aghaei et al., 2018; Cooper, 2008).**

Children are particularly vulnerable to T. canis due to soil consumption and contaminated vegetables **(Morimatsu et al., 2006; Yoshikawa et al., 2008 and Woodhall et al., 2014).** Infected children may be asymptomatic or show asthma symptoms **(Smith et al., 2009).** Detecting recent infections is crucial to prevent complications, as Toxocara larvae can cause granulomatous responses that impair organ function **(Sandra Guadalupe et al., 2021).**

Reliable serological techniques like ELISA with Toxocara excretory-secretory antigens (TES-ELISA) detect IgG antibodies effectively **(Noordin et al., 2005).** Research on recombinant proteins aims to enhance diagnostic accuracy while reducing costs and cross-reactivity compared to traditional TES production, with TES-30 and TES-120 showing high sensitivity and specificity **(Mohamad et al., 2009).**

Pediatric Asthma

Pediatric asthma is marked by variable airway limitation and persistent symptoms such as wheezing, coughing, shortness of breath, and chest tightness. Approximately 50% of infants wheeze in their first year, with most developing persistent asthma by age 6. The condition is influenced by genetic predisposition and environmental factors, with severity ranging from intermittent symptoms to life-threatening airway compromise **(Bush, 2019).**

Two groups of children exhibit wheezing: one with sporadic symptoms from viral infections, and another developing symptom later, often with atopy and family asthma history, suggesting a higher risk for persistent asthma. Predictive measures for long-term asthma risk remain limited **(Lizzo and Cortes, 2019).**

Epidemiology

Asthma causes more school absences and hospitalizations than any other chronic illness, affecting over 6 million (6.5%) children in the U.S. Its prevalence increases with age, from 1.9% in ages 0-4 to 7.7% in ages 5-14. Boys have a higher prevalence than girls, though the trend reverses in adulthood **(Lizzo and Cortes, 2019).** In Egypt, asthma prevalence among children aged 3-15 years is estimated at 8.2% **(Abdel-Baseer et al., 2017).**

Pathophysiology

Asthma involves inflammatory and resident airway cells, leading to airway inflammation and bronchial hyperresponsiveness **(Martin Alonso and Saglani, 2017).**

Toxocariasis

Toxocariasis refers to human infection by the roundworms Toxocara canis and Toxocara cati, found in dogs and cats, respectively **(Ma et al., 2018).** Adult Toxocara spp. live in the intestines, shedding eggs into the environment via feces. After embryonation, infective eggs can infect humans through accidental ingestion, with children at greater risk due to exposure in sandboxes and playgrounds. Upon ingestion, larvae hatch and migrate to soft tissues, causing various manifestations such as visceral larva migrans (VLM), ocular larva migrans (OLM), covert toxocariasis (CT), and neuro toxocariasis (NT) **(García-Rubio et al., 2023).**

Epidemiology

Toxocara spp. are widespread, particularly in regions with high dog and cat populations. In developing countries, seroprevalence can exceed 80% in children, while in the U.S., it ranges from 5% to 15%, with approximately 10,000 clinical cases reported annually. Risk factors include poverty, geographic location, contaminated soil, young age, and high pet populations, highlighting a prevalence gap between developed and developing nations (**Winders and Menkin-Smith, 2019**).

Life Cycle and Transmission

Toxocara canis has a complex life cycle (**Yoshida et al., 2022).** Adult worms in small dogs can produce up to 200,000 eggs daily, which become infective in 4–6 weeks. Upon ingestion, T. canis larvae migrate to the liver and lungs, where they may return to the intestine or remain dormant in tissues for years. Pregnant dogs can transmit larvae to puppies either in utero or through lactation **(Bowman, 2020).**

For T. cati, larvae also migrate similarly and are shed in feces 8 weeks post-infection. Unlike dogs, older cats may still experience tracheal migration. Cats can infect kittens during lactation but lack transplacental transmission **(Clark, 2021).**

Human Infection

Humans typically acquire Toxocara spp. Through ingesting eggs from contaminated soil or hands. Children are particularly vulnerable due to behaviors like geophagia. Other transmission routes include eating undercooked tissues from infected paratenic hosts (e.g., cows, chickens), larvae can survive in host tissues for up to 6 months **(Clark, 2021).** Direct contact with dog fur has been suggested as a potential infection source, but recent studies indicate a low risk from well-cared dogs **(Yoshida et al., 2022).**

Diagnosis of Toxocariasis

Clinical Signs

Symptoms depend on the organ affected, infection severity, and host response. They range from asymptomatic to non-specific which complicate the diagnosis. Risk factors, including exposure to soil, pets, and raw meat, should be considered **(Mazur-Melewska et al., 2020).**

Imaging

Ultrasound, Computed Tomography (CT), and Magnetic Resonance Imaging (MRI) help locate granulomas caused by migrating larvae. MRI is more sensitive for central nervous system involvement, showing hyper-intense areas on T2-weighted images (**Dietrich et al., 2020).**

Hematological and Biochemical Assessment

Persistent eosinophilia, hypergammaglobulinemia, and high total IgE levels suggest toxocariasis but are not definitive. Eosinophilia varies by organ involvement **(Yoshida et al., 2022).**

Serodiagnosis

ELISA and Western blot are primary tests, with ELISA showing 91% sensitivity and 86% specificity. WB, while more specific, is costlier. Cross-reactivity and persistent IgG antibodies complicate interpretation **(Noordin et al., 2020).**

IgE antibodies suggest active infection but are difficult to detect; however, IgG against third-stage larval antigens (L_3TES) differentiates acute from chronic infections **(Yoshida et al., 2022).**

Molecular Diagnostics

PCR can identify Toxocara species using unique ribosomal DNA markers, but biopsy-based methods are not practical due to the low worm burden (**Kaneva et al., 2020).** Bronchoalveolar lavage (BAL) fluid analysis in murine models suggests the potential for less invasive testing in humans with pulmonary disease **(Mazur-Melewska et al., 2020).**

Treatment of Toxocariasis

Anthelmintic Therapy

Albendazole is the first-line treatment due to its tissue penetration and ability to cross the blood-brain barrier. Typical dosing is 10–15 mg/kg/day for 5 days, though longer courses (4–8 weeks) have shown up to 78% efficacy in severe cases **(Kakimoto et al., 2019).**

Ivermectin is an alternative for patients with intolerance to albendazole, but it shows limited efficacy alone **(Del Giudice et al., 2018).**

Prevention and Control

Environmental Measures

Regular pet deworming reducing contact with contaminated soil and washing can prevent infection. Excluding pets from playgrounds and covering sandpits reduce environmental contamination (**Merigueti et al., 2022).**

Vaccine Development

Vaccine candidates derived from embryonated eggs and larval antigens show promise, but they are not yet available. Further research is needed to develop effective vaccines for both humans and animals **(Yoshida et al., 2022).**

Toxocariasis and Allergic Diseases in Children

Association with Asthma and Allergies

There is growing evidence linking toxocariasis to the development and worsening of allergic diseases, particularly asthma. Toxocara larvae trigger a Th2-skewed immune response, central to many allergic conditions. Improved diagnostics and public health measures focusing on hygiene and reducing environmental contamination could help reduce the impact of toxocariasis on allergic conditions **(Zibaei et al., 2019).**

Mechanism of Allergic Reaction

The allergic reaction to toxocariasis involves the migration of Toxocara larvae, leading to a type I hypersensitivity response. This is characterized by activation of Th2 cells and increased IgE production. Larvae provoke a strong eosinophilic response and release pro-inflammatory cytokines, causing tissue inflammation. This aligns with the mechanisms seen in asthma and allergic rhinitis **(Abou-El-Naga and Mogahed, 2023).**

Epidemiological Evidence

Epidemiological studies provide mixed results. In some regions, high rates of Toxocara IgG have been found in children with asthma and other allergic diseases. For instance, studies in Egypt show that many asthmatic children are seropositive for Toxocara IgG, suggesting a link between toxocariasis and asthma. However, this association is not consistent across all studies **(Sadri et al., 2019).**

Toxocariasis and Asthma

An infection with Toxocara may aggravate asthma, which is characterized by wheezing, hyperreactivity, and inflammation of the airways. According to research, the development of asthma may be aided by the allergic reaction to Toxocara larvae, which may exacerbate airway inflammation and allergen sensitivity **(Hanh et al., 2020).**

Clinical Evidence of Asthma Link

Studies have shown variable seroprevalence of Toxocara IgG in asthmatic children compared to controls. In Egypt, Toxocara seropositivity in asthmatic children ranges from 17% to 42%, while control groups report lower rates. These findings suggest Toxocara infection may be a factor in asthma, though results vary by region and study **(Badawey et al., 2018).**

Seroprevalence Studies

Elevated Toxocara IgG levels in asthmatic children support the hypothesis of a link between the infection and asthma. Differences in seroprevalence across studies could be due to geographical, environmental, or diagnostic variations, emphasizing the need for standardized diagnostic methods **(Khozime et al., 2019).**

Eosinophilia and IgE Levels

Eosinophilia and high total IgE levels are common in allergic diseases and have been linked to Toxocara infection. Elevated eosinophils and IgE indicate allergic inflammation, often seen in asthma patients. Research shows a significant relationship between eosinophilia, high IgE levels, and Toxocara seropositivity, suggesting a parasitic contribution to asthma-related inflammation (**Magnaval et al., 2020)**.

Respiratory Symptoms

Toxocara infection may lead to respiratory symptoms such as cough, wheezing, and dyspnea, which can resemble asthma. Severe instances, including eosinophilic pneumonia, have been documented, suggesting that Toxocara infection might worsen asthma symptoms and negatively affect respiratory health **(Mirza and Rathore, 2019).**

Diagnosis of Toxocariasis in Asthmatic Children

Diagnostic Challenges

Diagnosing toxocariasis in asthmatic children is difficult due to overlapping symptoms and challenges in detecting the parasite. ELISA for Toxocara IgG is commonly used but has

limitations, including cross-reactivity with other parasitic infections. Additionally, direct detection of larvae poses difficulties due to their small size and widespread distribution, rendering biopsy an unreliable method. **(Shamsian et al., 2019).**

Diagnostic Approaches

Serological tests combined with imaging, such as chest X-rays, improve diagnostic accuracy. X-rays can show respiratory abnormalities indicative of toxocariasis. PCR-based methods, while less common, are useful for confirming Toxocara species infection **(Fortini et al., 2023)**. ELISA, despite its limitations, remains the primary diagnostic tool, although its effectiveness varies with the infection stage **(Noordin et al., 2020).**

Preventive Measures

Preventive strategies involve educating the public about proper pet care and hygiene to minimize soil contamination, a key source of Toxocara transmission. Regular pet deworming and safe disposal of animal feces are also essential to preventing infection **(Santarém et al., 2023).**

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