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### **Migration and Autism Diagnosis**

#### Daina Crafa

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#### Abstract

Clinicians in many countries are increasingly working with children from migrant families. Although autism is diagnosed at an approximately equal rate in children in developed countries internationally (estimated 1% of the population), many studies report that children in migrant communities are at relatively higher risk for autism. Risk factors as well as symptom rates appear to vary across cultures. This chapter reviews the current state of the science and outlines conceptual considerations for clinicians assessing foreign, migrant, and minority children for diagnosis of autism. Possible reasons for higher rates among migrant children are discussed and suggestions for clinical evaluation are made.

**Keywords:** autism, migration, rates, risk factors, diagnosis, clinical assessment, culture, cross-cultural, heterogeneity, maternal migration, epigenetics, gene-environment interaction, symptom distribution, clinical measurements

#### 1. Culture hidden in plain sight

For many people, the word *autism* evokes images of Claire Danes or Dustin Hoffman portraying highly gifted, albeit socially affected, individuals. In reality autism spectrum disorder can be severely disabling, and are considered among the most common childhood psychiatric disorders affecting millions of children internationally each year [1]. They are a spectrum frequently marked by social impairment. Perhaps because of this characterization, the influences of the social world are not always included in discussions of autism diagnosis, although they may play a crucial role for determining whether a child is on the autism spectrum. Migration and cultural influences on social behavior in particular appear to impact autism diagnosis in critical ways, and may increase risk for developing autism as well as the potential for misdiagnosis. Moreover, children do not need to have migrated themselves to be affected, and can therefore be difficult to identify. This chapter will discuss the population and risk factors in detail and issue considerations and precautions for diagnosis.



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#### 2. Who is at risk?

Global migration rates have hit an all-time high within the current decade according to estimates made by the United Nations [2–4]. In several Middle Eastern countries, including the U.A.E. and Qatar, and Kuwait, more than 70% of residents are migrants. Among Englishspeaking countries, Canada and Australia have the highest percentages of foreign-born residents by population at more than 20% [5, 6]. Global rates of autism in migrants are not well documented. However, increasing migration rates may leave clinicians in many countries working with increasing numbers of children from migrant families.

Although autism spectrum disorder is diagnosed at an approximately equal rate in children internationally, numerous studies report that children of migrant communities are diagnosed with autism at higher rates than nonmigrant children [7]. Arguably the most famous and stillcited of these studies involved epidemiological surveys conducted by Christopher Gillberg's research group at the University of Göteborg in Sweden, each of which found higher rates of autism in migrant children [8–10]. The earliest of these studies identified higher rates of autism in urban children whose parents were born in "exotic" countries compared to children with parents born in Sweden. A population survey that examined cases specifically of autistic disorder that emerged across a decade of births also reported higher rates in migrant children. Likewise, their third study identified higher rates specifically in children arguably contributed to a new research trend: studying autism rates in children born locally whose parents (usually mothers) had migrated.

A series of studies performed in the U.K., which also emerged around the same time as the publications by Gillberg's group, provided supporting evidence for the emerging theory that autism was higher in children born to migrant families whether or not the children were born locally [11, 12]. The study by Goodman and Richards specifically found that first- and second-generation African-Caribbean children were diagnosed with autism at disproportionately higher rates [11], while Wing found higher rates of autism when the father's country of origin was outside the U.K. [12]. A study from Japan reported that migrants from one region of the country who moved to another region of the country also showed higher rates of autism, even though they had not crossed national boarders [13].

The migration theory of autism that emerged from these studies was initially crude—some authors proposed that genetic disorders or viral infections had been brought from the parent's homeland. One author famously later argued that no reasonable biological reason that autism would emerge after migration has been given [14]. The bulk of the findings supporting the migration theory of autism are from studies that are now decades old, and recent literature has suggested that the story may be more complicated. A few studies published within recent memory found no evidence that the child's immigration status played a role in rates of diagnosis [15].

Although a dearth of literature provides contemporary evidence for the migration theory of autism, a number of recent studies from around the world continue to report higher rates in locally born children whose parents have migrated [16–23]. The vast majority of these studies

have relied on national medical registries in countries such as Sweden or the Netherlands that record autism incidents along with family history, while several studies have additionally relied on census or survey reports.

Crafa and Warfa [24] compared autism rates of children born after their mothers migrated into predominantly Caucasian countries, and reported autism rates that were much higher than average compared to children whose parents were born locally. This review article examined population-wide rates in an effort to control for sample heterogeneity reported in by other similar articles.

One study considered whether maternal versus paternal migration status mattered, and only maternal status emerged as statistically significant [19].

Some of these studies have additionally provided possible biological explanations that are arguably well reasoned. Perhaps the most convincing reason is that stress caused by act of migration itself could increase autism risk by producing epigenetic changes in mothers who give birth after migrating to a new country or location, which echoes the state-of-the-art among the neurosciences as well [24]. This biological explanation will be detailed in the next section.

There are, of course, several contentions and caveats surrounding the maternal migration theory of autism. Different rates of autism appear to be prevalent in niche groups within a country. For example, Somali refugees in the U.S. state of Minnesota comprise a small community of refugees whose children have alarmingly high rates of autism (an estimated 1:28 children compared to the 1:68 estimated global average [25, 26]).

Something known as the Latina paradox defines one of the main ostensible challengers to the maternal migration theory of autism. Although most of the literature shows higher rates of autism in children with even one parent who migrated before their birth, several studies in the U.S. report lower rates of autism in children born in the U.S. with Hispanic parents who have migrated from Mexico [27, 28]. One review of maternal migration prior to birth likewise reported that children of all races and ethnicities who were born after maternal migration (including non-Hispanic Caucasian children) were more likely to have autism compared to children of their same race with locally born mothers, except for Hispanic children who were significantly *less* likely to have autism compared with their ethnic counterparts [24]. These findings suggest that there may be social or biological explanations, which will be explored in the next sections.

Few other research findings contradict the maternal migration theory of autism. One metaanalysis (commonly cited as potentially refuting the maternal theory of autism) reports that pregnancy complications increase risk of autism. This study reports specifically that "the elevated risk of autism among the offspring of women born abroad was just shy of statistical significance" [29]. However, it does not consider the role of ethnicity and includes some of the Hispanic studies mentioned above in its calculations. Although institutional racism and other obstacles to care could explain different diagnosis rates of certain minority communities, multiple epidemiological studies have reported that race does not appear to be a risk factor for autism among children from local families [29, 30].

#### 3. Biological theories of autism and migration

The biological relationship between autism and migration is currently somewhat of a mystery, and only a few contemporary theories have been proposed. Each of the proposed theories rely on the concept of a gene-environment interaction, which is exactly as it sounds—environmental factors interact with the genes of a fetus, child, or mother in some way that influences whether the autistic symptoms are expressed. Current theories disagree about the mechanisms of these interactions.

The example of HOXA-1 and rubella. Perhaps among the most famous recent attempts to explain the biological effects of maternal migration was made by Dyches et al. [31]. Echoing the earliest studies of migration and autism, which suggested that viral infections like rubella coming from the mother's home country could potentially increase autism risk [8–10], Dyches and her colleagues proposed that an interaction between viral infections and genetic susceptibility could potentially increase autism risk. They proposed as an example that an interaction between rubella and the widely studied HOXA1 gene may potentially explain higher autism rates in children born after their mothers' migrations. At the time the HOXA1 gene was considered a key potential candidate for causing autism, although continued study has failed to support a strong link to the disorder [32-34]. HOXA1 plays a role in early neural development and an allele variant on this gene was believed to be a possible precursor to autism. Dyches et al. proposed that having a genetic precursor, like a HOXA1 allele variant, alongside an environmental trigger might cause these mothers to have autistic children. They offer intrauterine rubella as an example of one potential environmental trigger that could affect children of migrant mothers [31]. Intrauterine rubella is believed to cause autism after an epidemic outbreak in the 1960s in the U.S. [31, 35]. Dyches et al. suggested that mothers might be at risk for having an autistic child if the HOXA1 variant is present and they are coming from countries where rubella is present or receive the vaccine for rubella during early pregnancy [31].

The scientific knowledge of autism has grown exponentially since the publication of their article in 2004. The take-away messages from their article withstand modern advancements. However, their example of HOXA1 and rubella no longer reflects the state of the art.

Although many promising studies of HOXA1 emerged from early studies, it appears to be rare and not the penultimate explanation initially thought [32, 36, 37]. While intrauterine rubella does affect central nervous system development and has been linked to autism [36, 38], there is no scientific evidence that rubella vaccines cause autism [39, 40]. Data reporting a link between vaccines and autism were determined to be falsified in 2011 [41].

Dyches et al. appear to have been onto something when they suggested that intrauterine changes caused by a gene-environment interaction could explain the emergence of autism after maternal migration. Although this was not their main point, findings over the past decade have accumulated demonstrating that poor intrauterine and pregnancy conditions increase the risk for autism.

*The epigenetics of pregnancy and migration*. Neuroscientist Daina Crafa and colleagues proposed that poor intrauterine and pregnancy conditions could be brought about by stressors related to migration [24]. They proposed that epigenetic processes explain the relationship between

these changes. *Epigenetic processes* refer to biological regulation of genes—while the genes a person has are fixed across their lifespan, epigenetic processes determine whether the properties of genes are expressed by turning them "on" and "off." Gene expression may change across a person's lifespan, and methylation is a primary mechanism of epigenetic changes to gene expression. Numerous studies have linked physiological stress with higher methylation during maternal imprinting (i.e., when genes are transferred from mother to fetus), poor intrauterine and pregnancy conditions, and autism [18, 21, 22, 29, 42–52].

Crafa and Warfa argue that circumstances surrounding the act of migration often produce substantial stress that could theoretically induce these epigenetic changes [24, 53]. Stressors potentially occur before or after migration, and may be quite varied. These could include war or trauma in the mother's home country or discrimination or acculturative stressors.

Their theory claims to account for the Latina paradox [24, 53]. Hispanic women included in several U.S. studies were significantly less likely to experience certain poor pregnancy or birth conditions compared with other ethnic groups, and this literature is where the term *Latina paradox* was originally born [54–56]. Some researchers have suggested that having a positive social network after migration could lower stress and therefore stress-related consequences, including autism [57–59]. Like the previous theory described in this section, it is based on careful literature review and has not been experimentally tested.

*The possible role of vitamin D.* Vitamin D (25-hydroxyvitamin D) is linked to cellular function and has frequently been investigated as a possible determinant for autism. Numerous studies have demonstrated that low vitamin D levels in a mother during pregnancy or her offspring during early childhood may predict autism risk; however, it is generally agreed that further research is necessary [60–63]. Several researchers studying maternal migration have hypothesized that mothers migrating from certain regions may carry lower levels of vitamin D and have higher rates of children with autism. While some studies have reported promising results, no study has yet demonstrated a link between vitamin D, maternal migration, and autism. Fernell et al. found that Somali mothers had lower levels of vitamin D compared with Swedish mothers whether or not they had an autistic child. They reported nonsignificant findings that Somali mothers with autistic children appear to have the lowest levels of vitamin D [64]. In a review of autism rates in the U.S., Dealberto reported higher rates of autism in "black" participants living in the U.S. as well as those who had migrated from Africa or the Caribbean, and hypothesized that this could be due to vitamin D levels, though the hypothesis was not directly tested [65].

#### 4. Cultural considerations for correct diagnosis

The clinical science surrounding autism and migration is still in its infancy. However, one message is becoming clear: children from diverse backgrounds are at greater risk for misdiagnosis. This section will review the current knowledge.

Although characterized by social impairments, autism spectrum disorder is robustly intertwined with the social world. The social cultures of both patient and clinician can influence who is diagnosed with autism, perhaps due to the heterogeneous nature of the disorder [66, 67]. Dr. Stephen Shore, professor and spokesperson on the autism spectrum, famously said, "If you've met one person with autism, you've met one person with autism" because the appearance of the disorder can be tremendously varied. The diverse nature of autism can sometimes be confused with other types of diversity to an untrained eye, and sometimes culture can look like autism and autism can look like culture. Both types of confusion disservice children of migrant families.

Children from foreign or minority families are sometimes diagnosed with autism later in childhood than their locally born counterparts [66]. There are multiple reasons for this, and confusing symptoms with cultural differences is one of them. In the absence of pronounced stereotype, social or communication deficits are sometimes mistaken for cultural differences. For example, a quiet child whose mother tongue is a foreign language may hesitate to speak because of language differences or because of poor language development. A child who avoids eye contact may not want to appear rude or may be showing signs of an undiagnosed malady. Social traits that are considered signs of autism in some countries may serve other social functions for foreign children.

In many "Western" countries, reduced eye contact is considered as one of the trademarks of autism. It is the earliest symptoms of autism to emerge during childhood, and clinicians in the U.S. and Western Europe often rely on it for diagnosis. It has been theorized that children with autism have "weak central coherence" which means that they look to the contextual information rather than the center of a scene and has been used to describe why children with autism avoid eye contact [68, 69].

However, in many Asian cultures, eye contact is considered rude and children are taught to avoid making eye contact [70]. Healthy children in multiple Asian countries have been found to exhibit "weak central coherence" (also called field-dependence) and some authors have asked whether Asian children can truly meet the criteria for autism that is used for diagnosis in the U.S. [71, 72]. Other studies reported that behaviors associated with autism were reported more often in healthy participants in Japan, India, and Malaysia compared with the U.K. [73]. However, a study of Korean children reported that similar social behaviors, including eye contact, were observed [72, 74]. A second study, which compared children from Israel, South Korea, U.K., and U.S., found that behaviors in the social domain remained stable across cultures although verbal and nonverbal behaviors and other symptoms varied by culture [75].

Although Asian studies seem to demonstrate similarities in the social domain, the international literature is more varied. German children showed lower social responsiveness and higher hyperactivity and conduct disorder compared to U.S. children [76]. Several studies report that children from Saudi Arabia display more externalizing behaviors compared to children from Jordan or the U.A.E. [77–79]. The few reviews of research in African children reports that symptoms may be comparable on the continent to "Western" diagnosis schemas, but the prevalence and distribution of these symptoms across children is uncertain [80, 81].

Diverse clinical presentations may lead to misdiagnosis in the clinic, and awareness of such cultural differences may help ensure diagnostic accuracy. Several studies have demonstrated

that using clinical diagnostic tools, such as the ADOS, may help reduce misdiagnosis in ethnic minorities and would potentially benefit children from diverse backgrounds, although these tools may not be universally optimal [82, 83].

#### 5. Other obstacles to obtaining diagnosis

In addition to cultural differences in the presentations of autism, several other factors may delay diagnosis for children from diverse backgrounds. In many countries, children from migrant families face obstacles to healthcare access. For example, healthcare may not be accessible or affordable. Parents may not be able to speak the local language and may not have access to or be aware of translation services [84–86]. A country's immigration policy may influence whether a family with an autistic child can seek help [87]. Moreover, vast arrays of medical models exist globally. Parents may be skeptical of autism or of the local approach to clinical practice. Some cultures may stigmatize autism or attribute it to incest [88]. The clinician is tasked with the difficult challenge of identifying these circumstances and assisting children in need.

#### 6. Closing remarks

Autism is a complex disorder that appears to traverse continents, although the symptoms of autism may vary in prevalence from one location to the next. Clinicians working with children from migrant families or who have been raised in rich cultural communities may need to utilize extra care when diagnosing.

Standardized clinical measures may facilitate the task of diagnosis. Additionally, clinical tools designed broadly for working with diverse patient groups may also be useful. The McGill Illness Narrative Interview, for example, is designed to act as an interview guide for clinicians who want to understand the cultural backgrounds of patients or their families [89]. Available in more than 10 languages, it may provide a framework that can be useful when talking to parents to understand the cultural background of a child from a migrant family.

As long as global migration rates remain high, in many countries clinicians are likely to encounter autistic children from migrant families. This chapter has aimed to provide an overview of the state of the art to help equip clinicians for these modern challenges.

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