ORIGINAL PAPERS / ARTICLES ORINAUX

HEALTH FACILITY-BASED PREVALENCE AND POTENTIAL RISK FACTORS OF AUTISM SPECTRUM DISORDERS IN MALI

PREVALENCE HOSPITALIERE ET FACTEURS DE RISQUE POTENTIELS DU SPECTRE DU TROUBLE AUTISTIQUE AU MALI

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Key words: ASD, prevalence, consanguinity, health facility

ABSTRACT

Background:

The prevalence of autism spectrum disorders (ASD) is 1-2% worldwide, 1 in 68 in the U.S, and unknown in Africa. ASD is under-diagnosed in Mali due to stigma and the lack of appropriate human resources and infrastructure.

Objective:

To determine the ASD frequency and potential risk factors in Mali.

Methods:

We identified all the health facilities and community-based organizations involved in the ASD diagnosis and management in Bamako. We established an ASD research and awareness platform in Mali, which encompasses

community-based organizations and a multidisciplinary team including psychiatrists, psychologists, pediatricians, geneticists, and public health and social science specialists. Through this platform, we performed a survey in health facilities and organizations where patients with ASD are likely to seek care in Bamako. We reviewed the psychiatric patient registry to obtain basic epidemiological profiles of children with ASD, epilepsy and other psychiatric disorders.

Results:

We found a health facility-based prevalence of ASD of 4.5% (105/2,343) in Bamako. The mean age at the first outpatient visit was 7.64 ± 3.85 years old. First degree consanguinity of 29.5% (31/105) was more frequent in parents of ASD children versus age and sex matched controls OR= 4.37 [1.96-9.76] p=0.0001.

Conclusion:

Our data suggest that ASD is more common than expected in Mali. The established ASD awareness and research platform may improve the diagnosis and management of ASD by raising ASD awareness, training of Malian clinicians and researchers in early ASD screening and diagnosis, and strengthening research capacity in genomics of ASD and other mental disorders.

INTRODUCTION

On average 1 in 68 children in the U.S. are diagnosed with autism spectrum disorders (ASD), but significant variations in prevalence depending on geographic area, sex, race/ethnicity, and level of intellectual ability exist (5). Autistic individuals have impaired reciprocal social interaction and communication, restricted repetitive and stereotyped behaviors (17). Girls experience fewer restricted and repetitive behaviors and externalizing behavioral problems (34). ASD are clinically classified by the severity of the disorder, language level, and the presence of learning disability/mental retardation (20). The onset or the diagnosis can be early around three years old or late in adolescence or adulthood (25). Comorbidities such as epilepsy, intellectual disability, and tuberous sclerosis are frequent (25, 32). A well-coordinated worldwide effort to identify risk factors for ASD and to meet the needs of persons with ASD and their families is needed from the global scientific community. Sub Saharan Africa (SSA) can significantly contribute in a unique way to a better understanding of the etiology, the genetic and environmental risk factors the influence of cultural backgrounds on ASD diagnosis and the preferences of treatment options based on parental perceptions (12, 16). However, ASD is currently understudied in Africa where its prevalence is unknown. More genetic epidemiology studies on ASD are needed in Africa in general and West Africa in particular (3). The University of Sciences, Techniques and Technologies of Bamako (USTTB), Mali, has been collaborating with the University of California Los Angeles, UCLA, U.S and the University of Cape Town (UCT), South Africa to establish an ASD genetic research platform and awareness in Mali for West Africa. Ultimately, such collaborative genetic research will lead to a better understanding of the genetics basis of ASD in populations with Black African ancestry in West Africa and elsewhere. In Mali, our aims were (i) to describe the landscape of ASD diagnosis and management (ii) to determine the health facility-based prevalence of ASD (iii) to implement our ASD awareness campaign across the country and (iv) to identify potential ASD risk factors.

METHODS

To describe the landscape of ASD and the health facility-based prevalence of ASD in Mali, we identified in 2014 all the public and private health facilities and organizations involved in the diagnosis and management of ASD in Bamako. We reviewed the outpatient medical charts of 12,000 children aged 3-14 years old treated at our study sites (the psychiatry department of the University hospital Point G, AMALDEME and three private medical clinics (Kaidara, Solidarite and Algi) from 2004 to 2014. We gathered information from 2,343 medical charts with neuropsychiatric disorders in our study questionnaire. Data were collected mainly by three junior investigators (a neuroscientist, a neurologist and a fourth year psychiatry resident) at our study sites. The following diagnostic criteria (the Diagnostic and Statistical Manual of Mental Disorders, DSM–5 for ASD (1), The International League Against Epilepsy, ILAE official report, 2014 for epilepsy (11) and the International Classification of Diseases, ICD-10 for other neuropsychiatric disorders (35)) by psychiatrists in the hospital, a neurologist at the private medical clinics Solidarite and Algi and by a neuro-

paediatrician at the private medical clinic Kaidara) were used in our study. We diagnosed autism spectrum disorder (ASD) on the basis of difficulties in two areas – social communication, and restricted, repetitive behaviour or interests according to the DSM-5 criteria. ASD cases were female or male children aged 3-14 years old and controls (epilepsy or other neuropsychiatric disorders) were age and sex matched. We selected two controls (one epileptic and one with another neuropsychiatric disorder) for each ASD case for risk estimation."

The psychiatry department of the teaching hospital Point G was our main study site. A weekly child outpatient visit (including autistic children) has now been running for a decade at the psychiatry department in Point G. Patients and their families benefit from the free psychological support and weekly music therapy (*Kotéba national)* conducted by the National Institute of Arts of Mali, under supervision of the medical psychologist.

In 2010 and 2013, the first two associations of autistic families were created.

To determine the health facility-based prevalence of ASD, we also contacted in Bamako every single health facility or organization involved in ASD diagnostic, care, awareness seeking collaboration.

To implement our ASD awareness campaigns, we have done various ASD awareness activities in urban and rural Mali. Since 2016, an ASD awareness conference is organized for the international autism day on April 2nd in Bamako. A 1-day seminary for information and education of parents of autistic children, traditional healers and medical doctors is held at the FMOS annually. A survey was conducted to determine the baseline knowledge, attitudes and practices (KAP) of Malians on ASD (AAS open, manuscript in review). To engage the decision-makers, we presented our ASD research program before the Malian House of Representatives in 2017 and the chief of the cabinet of the first Lady of Mali. Private and public media were associated heavily involved in our ASD awareness events from the beginning. In rural Mali, we took advantage of the existing health information system to reach out to the local population. In 2018, we designated the Autism Ambassadors and Animators of Mali whose task was to use their leadership and networking to raise the ASD awareness in the general population and among the decision and policy makers.

To identify the potential ASD risk factors, we calculated the odds ratio using the proportion of presence of a particular potential ASD risk factor in autistic children as compared to age and sex matched controls with either epilepsy or other neuropsychiatric disorders.

Our data were analyzed using SPSS20. The significance of the p value was set at <0.05. For the OR calculation, normal variant or absent of abnormality was used as the reference.

RESULTS

The health facility-based prevalence of ASD was 4.5% (105/2,343) in Bamako (**Table 1**). The male to female ratio was 1.5/1. A total of 86.7% (91/105) autistic children were from Bamako and 58.1% (61/105) were managed at the psychiatry department of the teaching hospital Point G. Autistic children were unschooled in 88.6% (93/105) of cases. On average, seven (7) autistic had the first medical visit each year (105 autistic children from 2004 to 2014) with the highest rates in 2009 (n=13) and 2012 (n=22) (**Table 2**). Autistic children were born to first degree consanguineous marriage and abnormal pregnancy four times as frequently as compared to children with epilepsy OR=4.47 [2.00-9.96] **p=0.0002** and OR=4.83 [1.02-22.91] **p=0.006,** respectively (**Table 3**). Autistic children were born to first degree consanguineous marriage and a multipara woman (>7 births) with a family history of psychiatric disorder on the paternal side two times as frequently as compared to children with epilepsy OR=2.72 [1.35-5.47] **p=0.0007,** OR=2.38 [1.06–5.33] **p=0.05** and OR= 2.97 [1.11-7.91] **p=0.04,** respectively (**Table 4**).

DISCUSSION

Health facility-based prevalence of ASD in Mali

In this study, we found 4.5% (105/2,343) autistic children in Mali (**Table 1**), a good estimation of the magnitude of ASD in Mali. In Nigeria, ASD was found to be among the least frequent infantile neuropsychiatric disorders with an incidence of 2.3% of 2,320 (2, 18). In one way, this is over-estimated due to study participant selection bias in our study sites where clinicians were either a child neurologist, child psychiatrist or a neuro-pediatrician. In another way, it may be underestimated because most parents do not seek care for their autistic children due to either the stigma surrounding autism or prefer traditional to the conventional medicine influenced by either local beliefs and ignorance or the difficult accessibility and unaffordability of available mental health services in Bamako. Consequently, the mean age at the first outpatient visit in our cohort was 7.64± 3.85 years old in Bamako (**Table 2**) as compared to the mean age at diagnosis of 3 years 10 months in the U.S. and 44.7 (Standard Deviation=21.2) months in Nigeria (18, 29). Rural, near-poor children and those with severe language impairment received a diagnosis 0.4 years later than urban children; 0.9 years later than those with incomes >100% above the poverty level and 1.2 years earlier than other children (29). The presumably delayed diagnosis of ASD in Malian children based on the mean age of first medical visit was a real concern. An earlier ASD screening and diagnosis coupled with early appropriate psychosocial intervention will definitely lead to a better outcome in Malian autistic children. Therefore, the modified checklist for toddlers–Revised/Follow up (M-CHAT-R/F) and the social communication questionnaire (SCQ) were validated into the Malian sociocultural context in Bamako in 2017 (23).

Autistic children were unschooled in 88.6% (93/105) (**Table 2**). Special education and behavior therapy are rare or absent in our resources limited settings (21, 24). Due to the lack of Applied behavioral analysis (ABA) services, atypical antipsychotic risperidone is widely prescribed to autistic children at the psychiatry of Point G (personal communication with the head department) to improve various behavioral problems as suggested in the literature (13).

On average, seven autistic had the first medical visit each year (105 autistic children from 2004 to 2014) with the peaks in 2009 (n=13) and 2012 (n=22) (**Table 2**). The peaks coincided with the year of creation of the two previous associations of parents of autistic children in Bamako. This suggests the importance of the active involvement of autistic parents to the ASD awareness campaigns to promote medical care seeking behaviors.

Potential ASD risk factors in Mali

From our retrospective study, we found that abnormal pregnancy, consanguinity, family history of psychiatric disorders were potential ASD risk factors in Mali. Children born to mothers from abnormal pregnancy OR: 4.83 [1.02-22.91] p=0.06 and those from consanguineous marriage OR= 4.47 [2.00-9.96] **p=0.0002** and those had four times were increased risk of being autistic as compared to their age and sex matched peers born to normal pregnancy by non-consanguineous couples. Exposures to environmental factors (alcohol, tobacco, cannabis, illegal drugs) during pregnancy as possible risk factors for autism have been investigated in numerous epidemiological studies with inconsistent results (19). The rate of consanguinity, a marriage between cousins or relatives, in the cohort of families with neuropsychiatric disorders ranges from 13% to 30% in Mali (7, 28, 30). Consanguineous families, with syndromic and non-syndromic autism will be worth investigating for the discovery of new recessive ASD genes in Mali.

When compared with vaginal delivery, either emergency or planned C-section has consistently been associated with an increased risk of ASD (4). The Malian government sponsored C-section to make it free all over the country in 2009 increasing drastically the C-section rate in the country (9). Consequently, Mali had an overall C-section rate in facilities of 31.0% from 2014 to 2016 (6). Despite such high rate, C-section was found in only 5 (4.8%) autistic versus 2 (1.9%) controls OR=2.5 [0.47-13.17] p=0.28 whereas Meguid *et al.,* 2018 reported C-section and neonatal jaundice as the most common risk factors of ASD in Egypt (22). Our main study site was the psychiatry department. We observed that pediatricians are more likely to inquire about C-section in caring for children as compared to psychiatrists. Psychiatrists focus more on the maternal mental health (31).

A family history of psychiatric disorder (when at least one person from either the maternal or paternal family had history of schizophrenia, bipolar disorder (33)) on the paternal side two times OR= 2.97 [1.11-7.91] **p=0.04 (Table 3).** Family history of mental illness may be more relevant in adolescent onset psychosis and a child is more likely to get a mental illness diagnosis in the presence of family history of psychiatric disorder (26). Lagunju *et al.,* reported 22.6% children (n=54) had a positive family history of autism, and 75.5% had associated neurological comorbidities (18). Besides co-morbidities, overlap between clinical manifestations of psychiatric disorders has been described in the literature (10, 28).

Mothers who had seven or more births were as twice as likely to have autistic children as compared to epileptic controls OR**=**2.38 [1.06–5.33] **p=0.05 (Table 4).** This could be explained by the advanced maternal age at the conception, but we did not gather information on the birth order of the autistic children in their respective families.

Implementation of ASD awareness campaigns in Mali

The Association *Djiguiya* in tandem the Autism Ambassadors and Animators of Mali including the ex-Ministry of higher education geared up the ASD awareness activities this year. Malian health authorities and significant stakeholders are on board to create a center for Autism Research and Training (CART) in Mali.

The landscape of ASD in Mali

As a result from describing the landscape of ASD in Mali, a multidisciplinary Malian ASD research team was built to generate preliminary data, to consolidate collaboration with foreign institutions such as the University of California Los Angeles (UCLA) and the University of Cape Town (UCT). A unified national association of parents of autistic children "Association *Djguiya*" was created in January 2018 to carry out ASD awareness activities and support ASD research in Mali. Due to our cultural representation of ASD in sub-Saharan Africa, most parents still prefer traditional and spiritual healing, partly due to the lack of appropriate treatment, and financial burdens of the conventional medical practice (8, 14, 15, 27). The *Kotéba national,* a psychotherapy technique designed based on the psychodrama of Jacob Levy Moreno (29) will be a good resource educating the general Malian population on ASD.

CONCLUSION

This study shows a high health facility prevalence of autism and a significant relationship to first degree relatives and to a paternal history of psychiatric illness. The important public health implications of these findings substantiate the detailed and unique methodology used in this study. This is a new development in ASD screening, diagnostic, care and research in Mali. Instead of "the same size fits all" policy for autistic children, the standard of ASD diagnosis and care has been raised in Mali far behind the systematic prescription of atypical and classic antipsychotic drugs to compensate for the lack of ABA specialists in Mali. The association "*Djiguiya*" took the ASD awareness campaigns with unexpected progress within year 1 of its creation. Our collaborative autism genetic research is new and unique in Africa and should inspire ASD and mental health researchers in neighboring countries. Our ultimate goal is to embrace the global autism awareness to establish a comprehensive autism research and training program in Mali for West Africa.

CONFLICT OF INTEREST

"The authors have declared that no conflict of interest exists."

ACKNOWLEDGMENTS

Thank you to Professor Kenneth H Fischbeck and Professor Peturs De Vries for their continuous support during this work.

FUNDING STATEMENT

"Dr. Modibo Sangare, MD, PhD was supported by a postdoctoral fellowship from a DELTAS Africa grant (DEL-15-007: Awandare). The DELTAS Africa Initiative is an independent funding scheme of the African Academy of Sciences (AAS)'s Alliance for Accelerating Excellence in Science in Africa (AESA) and

supported by the New Partnership for Africa's Development Planning and Coordinating Agency (NEPAD Agency) with funding from the Wellcome Trust (107755/Z/15/Z: Awandare) and the UK government. The views expressed in this publication are those of the author(s) and not necessarily those of AAS, NEPAD Agency, Wellcome Trust or the UK government." Dr. Modibo Sangare was also a grantee of the University of Sciences, Techniques and Technologies of Bamako, Ministry of Higher Education and Scientific Research of Mali.

Table 1: Health facility-based prevalence of neuropsychiatric disorders in Bamako, Mali

Diagnosis	Frequency (n=2,343)	Percentage (%)
Undetermined medical diagnosis	839	35.81
Epilepsy†	661	28.21
Mental retardation	125	5.33
Autism	105	4.5
Hemiplegia	99	4.22
Acute psychotic disorders	64	2.73
Schizophrenia	46	1.96
Mental instability	42	1.79
Personality disorders	36	1.54
Structural brain damage‡	34	1.45
Anxiety disorders	33	1.41
Depression	33	1.41
Language speech disorder	31	1.32
Symptomatic acute psychosis	31	1.32
Hysteria	26	1.11
Encephalopathy	24	1.02
Movement disorders§	16	0.68
Headaches	16	0.68
Obsessive-compulsive disorder	13	0.54
Cerebral palsy	10	0.43
Cannabis use related psychosis	10	0.43
Down syndrome	10	0.43
Sleep disorders	9	0.38
Rett syndrome	8	0.34
Mental confusion or delirium	7	0.30
Strabismus /nystagmus	6	0.26
Bipolar disorders	3	0.13
Suicide attempts	3	0.13
Attention deficit hyperactive disorders	3	0.13

†West syndrome (n=12), myoclonic seizures (n=5), etc… ‡Hydrocephalia (n=8), brain tumor (n=7), meningoencephalitis (n=7), brain malformation (n=5), head trauma (n=2), microcephalia (n=2), brain atrophy (n=2), hypoplasia (n=1), neurofibromatosis (n=1) §Cerebellar ataxia (n=9), dystonia (n=3), chorea (n=3), essential tremor (n=1)

Table 2: Socio-demographic information of the autistic children and their matched controls

Parameters		Autism N= 105 (100%)	Controls	
			Epilepsy N= 105 (100%)	Others* N= 105 (100%)
Sex	Male	63 (60%)	63 (60%)	63 (60%)
	Female	42 (40%)	42 (40%)	42 (40%)
Age group (years old)	< 4	12 (11.4%)	12 (11.4%)	12 (11.4%)
	4-8	38 (36.2%)	38 (36.2%)	38 (36.2%)
	9-14	55 (62.4%)	55 (62.2%)	55 (62.2%)
Address	Bamako	91 (86.7%)	81 (77.1%)	89 (84.8%)
	Provinces (regions)	14 (13.3%)	24 (22.9%)	16 (15.2%)
Study sites	Teaching Hospital Point G	61 (58.1%)	10 (9.5%)	52 (49.5%)
	AMALDEME	24 (22.8%)	0 (0%)	1 (1%)
	Private medical clinics	20 (19.1%)	95 (90.5%)	52 (49.5%)
Education	None	93 (88.6%)	79 (75.2%)	63 (60%)
	Primary school	12 (11.4%)	23 (21.9%)	40 (38.1%)
	Middle school	0 (0%)	3 (2.9%)	2 (1.9%)
Year of first outpatient visit**	2000 – 2005	3 (3%)	2 (1.9%)	4 (3.8%)
	2006 – 2008	21 (20%)	4 (3.8%)	20 (19.1%)
	2009	13 (12.4%)	5 (4.8%)	13 (12.4%)
	2010 – 2011	19 (18.1%)	38 (36.2%)	25 (23.8%)
	2012	22 (21%)	20 (19.1%)	20 (19.1%)
	2013 – 2015	27 (25.7%)	36 (34.3%)	23 (21.9%)

*Neuropsychiatric disorders different from autism and epilepsy **Year of first outpatient visit was the year when the patient was seen for the first time at one of our study sites. The mean age of patients at the first outpatient visit was 7.64 ± 3.85 years.

Table 3: Potential ASD risk factors in autistic versus epileptic children in Mali

Potential ASD risk factors		Autistic children (%) n= 105	Epileptic children (%) n= 105	Odds ratio (OR) p-value
Consanguinity	Yes	31 (29.5%)	9 (8.6%)	4.47 [2.00-9.96] **p=0.0002**
	No	74 (70.5%)	96 (91.4%)	
Pregnancy	Abnormal	9 (8.6%)	2 (1.9%)	4.83 [1.02-22.91] **p=0.006**
	Normal	96 (91.4%)	103 (98.1%)	
Delivery	C-section	5 (4.8%)	2 (1.9%)	2.5 [0.47-13.17] p=0.28
	labor dystocia	21 (21%)	10 (9.5%)	2.37 [1.06–5.33] p= 0.052
	Normal	79 (75.2%)	93 (88.6%)	
Infancy	Abnormal	32 (30.5%)	30 (28.6%)	1.09 [0.61-1.98] p= 0.88
	Normal	73 (69.5%)	75 (71.4%)	
Maternal family history of mental illness	Present	13 (12.4%)	8 (7.6%)	1.71 [0.68-4.32] p= 0.36
	Absent	92 (87.6%)	97 (92.4%)	
Paternal family history of mental illness	Present	16 (15.2%)	14 (13.3%)	1.17 [0.54-2.53] p= 0.84
	Absent	89 (84.8%)	91 (86.7%)	
Parity	Unknown	24 (22.9%)	45 (42.9%)	
	1-2	14 (13.3%)	9 (8.6%)	1.64 [0.68-3.98] p= 0.38
	3-4	26 (24.7%)	26 (24.7%)	1.00 [0.53-1.87] p= 0.86
	5-6	20 (19.1%)	13 (12.4%)	1.13 [0.56-3.55] p= 0.26
	7-15	21 (21%)	12 (11.4%)	1.77 [0.83–3.75] p=0.20

Table 4: Potential ASD risk factors in autistic versus neuropsychiatric disorders in Mali

Potential ASD risk factors		Autistic children (%) n= 105	Neuro-psychiatric disorders* (%) n= 105	Odds ratio (OR) p-value
Consanguinity	Yes	31 (29.5%)	14 (13.3%)	2.72 [1.35-5.47] **p=0.0007**
	No	74 (70.5%)	91 (86.7%)	
Pregnancy	Abnormal	9 (8.6%)	4 (3.8%)	2.37 [0.71- 7.94] p=0.25
	Normal	96 (91.4%)	101 (96.2%)	
Delivery	C-section	5 (4.8%)	2 (1.9%)	2.5 [0.47-13.17] p=0.28
	labor dystocia	21 (21%)	16 (15.2%)	1.39 [0.68–2.84] p= 0.47
	Normal	79 (75.2%)	87 (82.9%)	
Infancy	Abnormal	32 (30.5%)	21 (21%)	1.75 [0.93-3.30] p= 0.11
	Normal	73 (69.5%)	84 (79%)	
Maternal family history of mental illness	Present	13 (12.4%)	7 (6.7%)	1.97 [0.76-5.18] p= 0.24
	Absent	92 (87.6%)	98 (93.3%)	
Paternal family history of mental illness	Present	16 (15.2%)	6 (5.7%)	2.97 [1.11-7.91] **p= 0.04**
	Absent	89 (84.8%)	99 (94.3 %)	
Parity	Unknown	24 (22.9%)	38 (36.2%)	
	1-2	14 (13.3%)	23 (21.9%)	0.55 [0.26-1.14] p= 0.15
	3-4	26 (24.7%)	16 (15.2%)	1.83 [0.92-3.66] p= 0.12
	5-6	20 (19.1%)	18 (17.1%)	1.13 [0.56-2.30] p= 0.86
	7-15	21 (21%)	10 (9.5%)	2.38 [1.06–5.33] **p=0.05**

***other neuropsychiatric disorders different from epilepsy**

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