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Knowledge, attitudes and experiences of genetic testing for autism spectrum disorders among caregivers, patients, and health providers: A systematic review

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Abstract

BACKGROUND

Several genetic testing techniques have been recommended as a first-tier diagnostic tool in clinical practice for diagnosing autism spectrum disorder (ASD). However, the actual usage rate varies dramatically. This is due to various reasons, including knowledge and attitudes of caregivers, patients, and health providers toward genetic testing. Several studies have therefore been conducted worldwide to investigate the knowledge, experiences, and attitudes toward genetic testing among caregivers of children with ASD, adolescent and adult ASD patients, and health providers who provide medical services for them. However, no systematic review has been done.

AIM

To systematically review research on knowledge, experiences, and attitudes towards genetic testing among caregivers of children with ASD, adolescent and adult ASD patients, and health providers.

METHODS

We followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines and searched the literature in three English language databases (Pubmed, Web of Science, and PsychInfo) and two Chinese databases (CNKI and

Wanfang). Searched literature was screened independently by two reviewers and discussed when inconsistency existed. Information on characteristics of the study, characteristics of participants, and main findings regarding knowledge, experience, and attitudes of caregivers of children with ASD, adolescent and adult ASD patients, and health providers concerning ASD genetic testing were extracted from included papers into a charting form for analysis.

RESULTS

We included 30 studies published between 2012 and 2022 and conducted in 9 countries. Most of the studies (n = 29) investigated caregivers of children with ASD, one study also included adolescent and adult patients, and two covered health providers. Most (51.0%-100%) of the caregivers/patients knew there was a genetic cause for ASD and 17.0% to 78.1% were aware of ASD genetic testing. However, they lacked full understanding of genetic testing. They acquired relevant and necessary information from physicians, the internet, ASD organizations, and other caregivers. Between 9.1% to 72.7% of caregivers in different studies were referred for genetic testing, and between 17.4% to 61.7% actually obtained genetic testing. Most caregivers agreed there are potential benefits following genetic testing, including benefits for children, families, and others. However, two studies compared perceived pre-test and post-test benefits with conflicting findings. Caregivers concerns included high costs, unhelpful results, negative influences (*e.g.*, causing family conflicts, causing stress/risk/pain to children *etc.*) prevented some caregivers from using genetic testing. Nevertheless, 46.7% to 95.0% caregivers without previous genetic testing experience intended to obtain it in the future, and 50.5% to 59.6% of parents previously obtaining genetic testing would recommend it to other parents. In a single study of child and adolescent psychiatrists, 54.9% of respondents had ordered ASD genetic testing for their patients in the prior 12 mo, which was associated with greater knowledge of genetic testing.

CONCLUSION

Most caregivers are willing to learn about and use genetic testing. However, the review showed their current knowledge is limited and usage rates varied widely in different studies.

Key Words: Autism spectrum disorder; Genetic testing; caregivers; Child and adolescent psychiatrists; Knowledge; Experience; Attitudes

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Core Tip: More action should be taken to improve the knowledge level about genetic testing among caregivers of patients with autism spectrum disorder (ASD). Health education from health providers such as physicians and psychiatrists appear the most effective method. Improving the knowledge level of ASD genetic testing among health providers is necessary for better utilization of genetic testing in ASD practice. Caregivers of patients with ASD and patients themselves generally hold a positive attitude toward genetic testing. More comprehensive knowledge is needed to avoid potential misunderstandings.

INTRODUCTION

Autism spectrum disorder (ASD) is a group of severe neurodevelopmental disorders currently with limited treatment effectiveness[1]. The prevalence of ASD is around 1% but has been steadily increasing over the past two decades[2]. Diagnosis of ASD lacks objective biomarkers and primarily relies on subjective parameters such as clinical observation and evaluation of individuals' behavioral and developmental characteristics[3]. However, most patients are too young to express their feelings, clinical symptoms are complex and heterogeneous, not easily detected by parents and many patients do not receive timely diagnosis and treatment. This can lead to severe social dysfunction and heavy economic burden to families and society[4-6]. Although the specific etiology of ASD is unknown, it is widely accepted that both

genetic and environmental factors contribute to the pathogenesis of ASD. The estimated heritability of ASD ranges from 64% to 91%[7], and there are a large number of studies to elucidate the genetic mechanism of this disorder. Thousands of ASD risk genes carrying different kinds of mutations have been reported, such as rare *de novo* mutations, single nucleotide polymorphisms (SNPs), and copy number variations (CNVs)[8-10]. There are several comprehensive databases that aim to summarize all ASD risk genes and SFARI Gene (gene.sfari.org)[11] is one of the most well-recognized. SFARI Gene features a ranking system that gives users an estimate of the strength of the evidence in favor of each gene. For example, there are 232 genes with high confidence, which means these genes have been clearly implicated in ASD. As a result, several genetic testing techniques have been applied as an auxiliary examination tool when diagnosing ASD.

In clinical practice, genetic testing, such as Karyotype analysis, fluorescence in-situ genomic hybridization (FISH), fragile X testing, chromosome microarray analysis (CMA), and next-generation sequencing have all been utilized for ASD patients. Karyotype analysis was first used in the 1970s to identify extremely large CNVs[12] and FISH has been performed to identify submicroscopic CNVs since the 1990s[13]. In 2005, the American College of Medical Genetics and Genomics (ACMG) recommended karyotype analysis and FISH as standard testing for children with developmental delay or mental retardation, which included ASD[13-15]. For ASD with specific genetic causation, genetic testing could be utilized as the first-tier diagnostic tool. For example, 30%-50% fragile X syndrome caused by > 200 repeats of the CGG motif in FMR1 was shown to manifest as ASD[16]. In 2007, the American Academy of Pediatrics recommended Fragile X testing to be performed when ASD was diagnosed[17-19]. Given that ASD is polygenic, screening mutations genome-wide is necessary. CMA that could detect CNVs and SNPs across the genome has been increasingly used in the clinical practice of ASD[20]. The latest next-generation sequencing with higher resolution, including Whole Exome Sequencing (WES) and Whole Genome Sequencing could be used to detect single nucleotide variants, indels and other variants in patients[21]. CMA and WES have been recommended as the first-tier clinical diagnostic test for individuals with developmental disabilities,

including ASD by the ACMG in 2010 and 2013, respectively[12,22]. So far, the clinical diagnostic yield of CMA and WES for ASD was 9.3 to 24.1%[23], and 8.4% to 15.4%[24,25] respectively.

There are many potential benefits of genetic testing for patients with ASD and their families, including promoting early diagnosis and intervention, identifying etiology, reducing medication compliance, providing scientific suggestions for parents' fertility planning, and reducing parents' guilt and anxiety[26,27]. However, the usage rate of genetic testing varies dramatically across countries and regions. As far as we know, the highest rate of receiving any type of genetic testing was reported in France in 2014 (61.7%)[28]. Much lower rates were reported in America in 2020 (17.4%) and Malaysia in 2022 (19.8%)[29,30]. Even within the same country in the same year (for example, America in 2018), rates ranged from 28.0% to 57.1%[31,32]. This could be due to several factors. First, genetic testing does not always identify pathogenic variants ~~as~~ because the complex genetic architecture of ASD is still not fully understood[33,34]. Second, a positive finding from genetic testing is not always helpful in clinical management. Third, the test is costly for some families[31]. Furthermore, the usage rate of genetic testing is affected by awareness and attitudes of both caregivers and health providers who are involved in the diagnosis and care of children with ASD, especially child and adolescent psychiatrists (CAP)[31,35]. In a previous study, 67.5% of parents reported that the main reason why they did not get genetic testing was they did not receive suggestions from physician[36].

To maximize the benefit of genetic testing in ASD clinical practice, it is very important to understand caregivers' and health providers' opinions towards genetic testing for ASD. To date, several studies have investigated knowledge, experiences, and attitudes toward genetic testing for ASD. In the present article, we systematically reviewed the literature published up to October 2022 to outline the current state of knowledge level, experiences, and attitudes toward ASD genetic testing among caregivers of children with ASD, adolescent and adult ASD patients, and health providers. In addition, to summarize factors related to the underutilization of genetic testing and provide a direction for future improvement.

MATERIALS AND METHODS

Literature search

We searched the literature in 3 English databases (Pubmed, Web of Science, and PsychInfo) and 2 Chinese databases (CNKI and Wanfang). The search items were (caregivers* OR caretakers* OR parents* OR psychiatrist* OR specialists*) AND (autism spectrum disorder OR ASD* OR autism* OR autistic) AND (genetic testing OR genetic assessment OR genetic risk assessment) AND (knowledge* OR awareness* OR perception* OR attitudes* OR experiences* OR utilization* OR utility* OR interest*). The final search was done on October 7, 2022, and searched literature was exported to Endnote X9.

Inclusion and exclusion criteria

Peer-reviewed articles that met all the following criteria were included in our research: (1) the targeted disease was ASD; (2) participants were either caregivers of children with ASD, adolescent and/or adult ASD patients, or health providers who provided medical services for them; and (3) the article focused on evaluating the knowledge, experiences, or attitudes about ASD clinical genetic testing. Articles were excluded if: (1) participants other than the target population described above were included; (2) none of the three topics of interest was covered; (3) the study focused on prenatal genetic testing; (4) the article was not written in English or Chinese; (5) the study was a review; or (6) full-text was unavailable.

Selection of sources of evidence

We first screened the searched papers by reading titles and abstracts. Then, full texts of the remaining studies were read and those that met the eligibility criteria were included for further study. These two steps were carried out by two independent reviewers. When there was non-conformity, a discussion was organized, and a senior reviewer was invited if necessary. The whole process of selection was displayed in the PRISMA flowchart (Figure 1)[37].

Data charting process

Relevant information of included papers was extracted into a charting form, including (1) characteristics of the study (author affiliation, country, year of publication, time period(s) of the study, study setting, sample size, sampling method, survey methods, and tools); (2) characteristics of participants (age of child at diagnosis and at survey time, financial insurance of child, relationship with ASD patients, age, gender, marital status, educational level, annual income, current employment status, number of children, number of children with ASD, and family history of ASD) of the participants; and (3) main findings of the study (knowledge, experience, and attitudes concerning ASD genetic testing). The details were displayed in supplementary materials. After reading all 30 included articles and discussing them, a coding instruction was summarized by two reviewers. The data were then extracted by one reviewer and checked by another reviewer.

RESULTS

Search results

The original search yielded 483 records. After removing duplications and screening abstracts, 78 remained for full-text screening, after which, 30 records were included. Reasons for exclusion were a. inclusion of subjects other than the target population, for example, caregivers of patients with developmental disorders other than ASD, such as intellectual disability, developmental disorder (n = 16), general population (n = 16); b. not covering any of the three topics of our interest (n = 5). The process of article selection is displayed in Figure 1.

Characteristics of studies

Among the final included 30 studies, 20 (66.7%) investigated knowledge, 17 (56.7%) investigated experience, and 22 (73.3%) investigated attitudes toward ASD genetic testing. They were published between 2012 and 2022, and conducted in 9 countries, with 19 (63.3%) in United States. More than half (n = 17, 56.7%) utilized convenience sampling. Other sampling methods included purposive sampling (n = 6, 20.0%), random sampling (n = 3, 10.0%), and snowballing sampling (n = 3, 10.0%).

Investigating methods included online surveys (n = 16, 53.3%), face-to-face interviews (n = 9, 30.0%), and telephone calls (n = 7, 23.3%). The most frequently used instrument was a questionnaire with open-ended questions (n = 14, 46.7%). Some instruments included both close-ended and open-ended questions (n = 7, 23.3%), or only close-ended questionnaires (n = 7, 23.3%). More details can be found in Table 1. A standard questionnaire which was defined as a questionnaire with focused themes and standard evaluating methods and could be utilized by other researchers with a similar research purpose was used in two studies—Perceptions of ASD Genetic Testing Survey developed by Zhao *et al*[38] and The Centers for Autism and Related Disabilities developed by Cuccaro *et al*[39].

Characteristics of participants

The majority of the studies (n = 29, 96.7%) investigated parents of children with ASD, including 23 (75.9%) that only covered parents, 4 (13.8%) that also covered other caregivers[27-29,31], one also included health providers[32], and 1 (3.4%) that included adolescent and adult patients[40]. Only one study investigated CAP alone[41]. The sample size of the 30 included studies ranging from 20 to 1444. Of 19 studies that provided gender information, 60%[35] to 95%[42] of the participants were female. Of 13 studies that reported the mean age of parents, these ranged from 37.4[36] to 46.7[43]. Of 8 studies that reported the marital status of parents, 81.3%[44] to 92.3%[45] were married or living as married. Of 8 studies that investigated current employment status, 51%-71.1% of caregivers were employed. Of 16 studies that provided information about the educational level of caregivers, 21.0%-69.4% had a college or higher degree. The lowest educational level of parents was reported in 2 studies that only involved parents of children with ASD who had taken CMA testing[46,47].

Age information of children with ASD was provided in some studies, including 7 (24.1%) that reported mean current age ranging from 5.2 to 16.5 years old[26,43] and 5 (16.7%) that reported mean age at diagnosis ranging from 3.0[29] to 4.7[48] years old. Among 7 studies that reported the number of children with ASD, most families (17.8%-93.7%) had only one child with ASD, while 5.9%-17.9% of families had two or

more children diagnosed with ASD. Of 7 studies that addressed family history, 10.5%-34.6% of participants had a positive family history of ASD.

Knowledge, experiences, and attitudes

Specific questions related to the three topics of interest were (1) Knowledge: perceived cause(s) of ASD, knowledge about genetics and genetic testing, pathways to acquire such knowledge, and information needs prior to genetic testing; (2) Experience: experience of being referred to genetic testing and using genetic testing; and (3) Attitudes: why participants supported genetic testing and their concerns about genetic testing; for participants who have not done genetic testing, their intention to pursue genetic testing in the future; for participants who had done genetic testing, their satisfaction with ASD genetic testing and willingness to recommend genetic testing to others (Table 2).

Knowledge of genetics and ASD clinical genetic testing among parents and other caregivers: In total, there were 7 studies that surveyed the perceived cause(s) of ASD of the parents and other caregivers. These studies found that 51.0%-100% of the them thought ASD was partly or fully explained by genetic factors, and 11.9%-12.0% thought ASD was entirely explained by genetic factors. Parents who believed that their child's ASD was permanent tended to attribute ASD to genetic factors[16]. One study reported parents' understanding of genetics: parents stated that they were familiar with and knew the meaning of DNA (94%), genes (92%), chromosomes (86%), genetic testing (87%), and CMA (21%)[39].

In addition, there were 14 studies that investigated caregivers' knowledge of genetic testing for ASD. Of seven studies that asked them whether they were aware of ASD genetic testing before the study, 17.0% to 78.1% answered yes[29,49-54]. However, one study reported that 95% of the participants said they did not know what genetic tests can test[26]. Furthermore, in one study of participants without genetic testing experience conducted in Sweden in 2020, only 16.2% of parents and 19.6% of autistic adolescents and adults believed that genetic testing for ASD was available[40]. There were three studies from the same team using the same seven-item

questionnaire about knowledge of ASD genetic testing. In this questionnaire, wrong and correct answers were scored 0 and 1, with a total score ranging from 0 to 7. The three studies were all performed among parents with children with ASD from United States in 2019. The mean score for those studies were 2.4 ± 1.2 (n = 411), 2.5 ± 1.2 (n = 552), and 2.5 ± 1.2 (n = 443), respectively[18,24,26]. Caregivers' knowledge of ASD genetic testing was positively associated with their educational level, the number of children with ASD, and socioeconomic status, and negatively related to the severity of the child's ASD diagnosis[52,54,55]. Furthermore, caregivers who had visited a genetic service and who had received information from physicians rather than other sources also had a higher level of knowledge[55,56].

In 4 studies that reported the pathways through which the parents had acquired knowledge about ASD genetic testing, 18.3%-57.7% of the participants received related information from physicians[49,50,54,55]. Other main resources include the internet or mass media (23.9%-45.7%)[50,54,55], ASD organization or support groups (12.0%-42.9%)[50,54,55], and other parents of children with ASD (17.0%-36.4%)[50,54,55]. Two studies reported what information parents wanted to know to improve their knowledge about genetic testing. This information included: accuracy of genetic testing (38% and 88.4%), cost (60.0% and 85.9%), benefits of genetic testing (48.0% and 83.8%), testing procedure (29.0% and 77.8%), eligibility to undergo genetic testing (62.4%), potential harms caused by genetic testing (29.0% and 56.1%), previous use and experience among individuals affected by ASD (50.8%), and confidentiality issues (12.0% and 48.0%)[53,55].

Experiences of ASD clinical genetic testing:

Parents and other caregivers: Three (10.0%) of the 30 studies only included parents of children with ASD who had undergone CMA testing, and one only included parents who had been offered any genetic testing for their child with ASD. Among the remaining studies, 6 reported that 9.1% to 72.7% of caregivers and 2.8% of autistic adolescents/adults[40] had been referred to genetic testing, and 13 (43.3%) studies reported rates of using any type of genetic testing ranging from 17.4% in United States[29] to 61.7% in France[28]. Regarding specific types of genetic testing,

fragile X testing was most widely used by parents, with utilization rates ranging from 4.4% to 39.2%[36,39,49,56]. The utilization rates of CMA and karyotype tests were 7.4%-13.1%[49,56], and 0.7%-37.6%[36,49,56], respectively. Only one study in Jordan reported that the usage rate of WES was 3.3%[36]. The associated factors of caregivers' usage of genetic testing were reported in 4 studies. Those who had a higher awareness level of genetic testing[49], who received related information from healthcare providers rather than other sources[31,49], who had visited geneticists[31,56], and those with higher household income[36] were more likely to conduct genetic testing for their child.

Health providers: Only one study was of CAP and was performed in United States in 2021. It showed that 54.9% of respondents had ordered ASD genetic testing for their patients in the prior 12 mo. Psychiatrists who accepted a higher percentage of ASD cases, who had more knowledge about genetic testing and higher perceived utility of ASD genetic testing, and who were at a University medical center were more likely to request genetic testing for their patients with ASD; participants with more years of working experience tended not to order genetic testing for their patients with ASD[41].

Attitudes towards ASD clinical genetic testing:

Parents and other caregivers: There were 15 surveys among caregivers which reported participants' reasons for supporting genetic testing. Reasons could be categorized into three groups: (a) Benefits for the child, including getting better intervention (n = 13), finding out the cause(s) of ASD (n = 11), getting a definitive diagnosis (n = 8), getting a better understanding of their condition (n = 6), and additional resources (n = 5); (b) Benefits for family and parents, including helping with family planning (n = 8), and future reproductive decisions (n = 5), identifying risk of associated children (n = 2), and reducing stigma (n = 1); and (c) Benefits for other people, including promoting scientific research (n = 6), and providing an indication for other children with ASD (n = 1) (Figure 2A).

Of caregivers who had taken their child for genetic testing, more than half held positive attitudes toward their experience of genetic testing, reporting that genetic

testing had been helpful for their child and their family[29,46,49]. Getting additional resources (81.8%), getting a definitive diagnosis (81.8%), contributing to scientific knowledge (61.8%), identifying associated medical risks (25.0%), playing a role in future reproductive decisions (19.1%), helping with treatment planning (12.5%, 16.2%, 90.9%), gaining a better understanding of the child (10.3%), finding a cause of ASD (10.3%, 12.5%), and helping with family planning were reasons why they thought genetic testing was useful[29,31,46,49]. Two studies compared perceived benefits between caregivers, one who had taken their children for genetic testing and the other who never had. The first showed that the post-test group had more positive attitudes toward ASD genetic testing[31], the second reported less positive attitudes[27].

There were 15 studies that reported caregivers' concerns about genetic testing. They can be divided into four areas: (a) high cost (n = 6); (b) useless results: would not provide any useful information (n = 9), would not help with treatments (n = 5), and would not make changes to daily life (n = 4); (c) negative influences: would cause family conflicts (n = 4), would cause stress/risk/pain to children (n = 3), cause parental concern (n = 2), would do more harm than good (n = 2), and contradict their religious or cultural beliefs (n = 1); would cause discrimination when buying financial insurance (n = 3) and public discrimination (n = 1); and (d) other: the test had poor validity (n = 1) (Figure 2B). Four studies reported concerns of participants who had taken their child to genetic testing: lack of detailed information and did not help with further treatment and financial costs were the main reasons for dissatisfaction[26,40,44,49]. Parents' attitudes towards genetic testing were positively related to their perceived severity of ASD[57] and negatively related to their perceived barriers in conducting genetic testing[57], and parents' age and educational level[52].

There were 8 (26.7%) studies which reported that 46.7%[54] to 95%[56] of caregivers without previous genetic testing experience intended to pursue genetic testing in the future, and 2 studies showed that 50.5% and 59.6% parents who have purchased genetic testing services for their children would recommend genetic testing to other parents. It is reported that parents' willingness to pursue genetic testing for their

children with ASD was positively associated with their attitudes towards genetic testing, their perception of other people's opinions, and their self-efficacy in pursuing genetic testing[57].

Health provides: Only one survey among CAP reported why they order genetic testing for their patients. The main reason is to diagnose ASD and reported by 59.9% of those who had ordered a genetic testing in the prior 12 mo[41].

DISCUSSION

To the best of our knowledge, this is the first study that systematically reviewed caregivers', patients', and health providers' knowledge, experiences, and attitudes toward genetic testing for ASD. We searched the related literature without area and time limitations, extracted, and analyzed information from 30 studies. We found that most caregivers agreed that genetic mutations are causes of ASD and knew a little about ASD genetic testing but lacked a deeper understanding of the tests. Caregivers can obtain information about ASD genetic testing from several sources, including physicians, the internet, ASD organizations, and other caregivers of ASD patients. Most obtained information from non-professionals, although obtaining information from professionals contributes to better knowledge and more willingness to use ASD genetic testing. The usage rate of ASD genetic testing is generally low and varied dramatically among studies, even within the same country in the same year, as did the rate of being referred for ASD genetic testing by health providers. In addition, caregivers generally held positive attitudes toward genetic testing. More than half of the parents who had used genetic testing would recommend it to other parents and 46.7% to 95% of caregivers without previous genetic testing experience intended to pursue genetic testing in the future.

Although it is repeatedly reported that awareness level of genetic testing was closely associated with its usage rate and users' attitudes[41,49,56,58]. the awareness level of ASD genetic testing among both caregivers and health providers was not ideal. Most caregivers had heard a little about genetic testing, but few of them had a deep understanding. For example, less than 5% knew the diagnosis rate/yield of ASD genetic testing and the legitimate rights of children with ASD[57]. In contrast,

over half of participants showed an interest in gaining more knowledge about genetic testing[55]. This indicates that caregivers generally have limited access to such knowledge. Given that a variety of methods to obtain relevant knowledge have been reported, the problem of the low knowledge levels among caregivers can easily be resolved if appropriate actions are taken.

Health providers, such as physicians and psychiatrists are key to improving the knowledge level of caregivers about ASD genetic testing because parents who acquire genetic information from them were more likely to agree to genetic testing[27,46]. However, most parents did not receive such knowledge from their health providers. For example, one study reported that only 35.3% of parents who were aware of genetic testing received information from their physicians[55]. In addition, another study, not included in our review, reported that more than half of caregivers had not received any additional information about ASD from their physicians following diagnosis, let alone knowledge about genetic testing[59]. This may be linked to lack of knowledge about screening and diagnosis of children with ASD among physicians[60]. A previous study reported that about half of pediatricians who had cared for children with ASD did not know the clinical guideline regarding genetic testing for children with ASD[61]. It is possible and of concern that physicians who know related guidelines may not comply with them. This could result in even lower usage rate of genetic testing[62]. Not receiving doctors' recommendations was also an important reason why ASD genetic testing usage rate was low[46]. Only 18% of physicians would recommend genetic testing to all children with ASD[61]. Physicians should be encouraged to learn more about genetic testing. They can also recommend genetic counseling to patients, which could help to increase parents' awareness level about genetic testing[30].

Although genetic testing is more widely approved and prices are decreasing, the usage rate has not recently increased. For example, in United States, the usage rate was 17.4% in a survey conducted in 2018, whilst four years earlier the rate was 57.1%[29,32]. The usage rate of 57.1% was reported in a survey in Washington[32]. As the capital of the United States, Washington is economically more developed than other regions in America, which contributes to a higher usage rate. The usage rate

differed dramatically among different areas. The usage rate of any type of genetic testing was 19.8% in Malaysia in 2022, which was much lower than that in Spain in 2017 (51.0%) and in France in 2012 (61.7%)[28,30,56]. This might be caused by different level of economic development. Also, a study reported large difference in usage rate of genetic testing between America and France, with 27.8% in America and 61.7% in France[28]. The free access to care in France may be associated with higher compliance with genetic testing recommendations[28].

Although most caregivers agreed with the benefits of ASD genetic testing and expressed positive attitudes towards future testing, many concerns still exist which prevent them from seeking genetic testing. The most frequently reported concern was that they thought genetic testing would not provide any useful information for them and could not help with further treatment. This was also an important explanation for why they were unsatisfied with genetic testing[44]. Parents may hold high expectations, hoping test results bring a definitive diagnosis and etiology of ASD[44,49]. However, only 35% of ASD cases had genetic abnormalities, and about 80% of cases received negative results from CMA testing[25,46]. Visiting genetic counselors should also be encouraged before and after testing to help caregivers make an informed decision, understand, and use testing results more wisely[63]. Besides, the high cost of genetic testing and lack of insurance were also important reasons why genetic testing was underutilized. A study in Jordan indicated that 72% of families reported overall costs of CMA and fragile X testing constituted over 30% of their annual income, and lack of testing resources and insurance coverage further increased the financial burden[36]. However, in the long term, genetic testing may promote an earlier diagnosis and improve the prognosis of children with ASD, consequently, saving future costs[25]. Governments are therefore encouraged to offer affordable genetic testing. For example, government-funded CMA tests are freely available for children diagnosed with ASD in Israel[25]. However, genetic testing results can cause negative emotions for parents and children. For example, some parents believed that they would be blamed or discriminated against if the ASD was verified as inherited from one of them[51], the testing procedure, especially blood draws, would make their child uncomfortable, and the stigma attached to mental

illness would increase their level of stress[43,52]. Genetic counseling before and after testing is therefore necessary to minimize misunderstanding about genetic causes and psychological or marriage counseling may need to be considered to alleviate negative emotions.

There were some limitations in this systematic review. Firstly, published research was limited and mainly concentrated in United States and other developed countries. Understanding implementation of ASD genetic testing in low and middle-income countries could not be achieved from this review. Secondly, only two studies targeted health providers. Because it is one of the most effective ways to impart knowledge about genetic testing to caregivers, it is very important to understand both health providers' understanding and attitudes toward genetic testing. Furthermore, there was little uniformity in instruments used in studies lack uniformity making it difficult to synthesize and compare results.

Clinical implications

Firstly, more actions should be taken to improve the knowledge level of genetic testing among caregivers of patients with ASD. Health education through health providers, like physicians and psychiatrists, is the most effective way. Secondly, improving the knowledge of genetic testing among health providers is necessary for better utilization of genetic testing in ASD practice. Thirdly, caregivers of patients with ASD and patients themselves generally hold a positive attitude toward genetic testing. More comprehensive knowledge is needed to avoid potential misunderstandings.

CONCLUSION

The usage rate varied widely in different studies. It is mainly affected by the knowledge level of related parties. However, the review showed that although most caregivers are willing to learn about and use genetic testing, their current knowledge is limited.

ARTICLE HIGHLIGHTS

Research background

The popularity of genetic testing for patients with autism spectrum disorder (ASD) varies dramatically across countries. It is highly dependent on the knowledge, experiences, and attitudes toward genetic testing among caregivers of children with ASD, adolescent and adult ASD patients, and health providers. As a result, many related studies have been conducted worldwide but no systematic review has been done.

Research motivation

Getting a better knowledge of factors that are associated with the usage rate of genetic testing for patients with ASD has the potential to maximize the benefits of the test for patients.

Research objectives

To systematically review research on knowledge, experiences, and attitudes towards genetic testing among caregivers of children with ASD, adolescent and adult ASD patients, and health providers.

Research methods

We conducted a systematic review by searching the related literature without area and time limitations in both English language and Chinese language databases.

Research results

In 30 studies conducted in 9 countries,17.0% to 78.1% of caregivers/patients were aware of ASD genetic testing. However, they lacked a full understanding of it. Between 9.1% and 72.7% of caregivers in different studies were referred for genetic testing, and between 17.4% and 61.7% actually obtained genetic testing. Among caregivers, 46.7% to 95.0% without previous genetic testing experience intended to obtain it in the future, and 50.5% to 59.6% of parents who previously obtained genetic testing would recommend it to other parents. In a single study of child and

adolescent psychiatrists, 54.9% of respondents had ordered ASD genetic testing for their patients in the prior 12 mo.

Research conclusions

The usage rate varied widely in different studies. It is mainly affected by the knowledge level of related parties. However, the review showed that although most caregivers are willing to learn about and use genetic testing, their current knowledge is limited.

Research perspectives

Firstly, more actions should be taken to improve the knowledge level of genetic testing among caregivers of patients with ASD. Health education through health providers, like physicians and psychiatrists, is the most effective way. Secondly, improving the knowledge of genetic testing among health providers is necessary for better utilization of genetic testing in ASD practice. Thirdly, caregivers of patients with ASD and patients themselves generally hold a positive attitude toward genetic testing. More comprehensive knowledge is needed to avoid potential misunderstandings.

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PRIMARY SOURCES

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2	Cuccaro, Michael L., Kayla Czape, Michael Alessandri, Joycelyn Lee, Abigail Rupchock Deppen, Elise Bendik, Nicole Dueker, Laura Nations, Margaret Pericak-Vance, and Susan Hahn. "Genetic testing and corresponding services among individuals with autism spectrum disorder (ASD)", American Journal of Medical Genetics Part A, 2014. Crossref	17 words — < 1%
3	www.researchgate.net Internet	17 words — < 1%
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