Mortality and Factors Associated with Death in Autism Spectrum Disorders - a Review

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Received 30 August 2012; Published online 26 January 2013

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Abstract

The purpose of this review is to provide information on mortality and factors associated with death in people with autism spectrum disorder (ASD). A review of the published systematic mortality studies suggest that the observed number of deaths is nearly three times higher in populations with ASD than in the general population. Research into risk factors associated with survival in people with ASD is limited, and no studies have controlled for changes in these factors over time. The most important risk factors that are associated with reduced life expectancy in people with ASD are moderate to profound intellectual disability, having epilepsy, and female gender. This supports the need for continuous and coordinated care for this high-risk sub population of individuals within the population of people with ASD. It is concluded that measures to reduce inequalities in people with ASD need to focus on reducing mortality from potentially preventable causes of death such as infectious diseases and accidents.

Keywords: Autism spectrum disorders; Mortality; Standardized mortality ratio; Avoidable mortality

1. Introduction

In ICD-10 (WHO, 1992) and DSM-IV (APA, 2000) pervasive developmental disorders (PDD), are terms for a group of developmental disorders characterized by atypical development in socialization, communication and behavior. Sensory processing abnormalities leading to an over- or underreaction to stimulation are a marked problem in some individuals with PDD (Leekam et al., 2007), although they are not an essential diagnostic criterion for PDD. Owing to the variety and grade of its characteristic features and associated symptoms among patients, PDD is now generally referred to as autism spectrum disorders (Ozonoff, 2012).

Autism spectrum disorders (ASD) usually are diagnosed in early childhood. Accumulating evidence suggest that ASD occurs in approximately 1% of the population (Prevalence of Autism Spectrum Disorders – Autism and Developmental Disabilities Monitoring Network, United States, 2006,

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2009), with more males than females receiving a diagnosis (Baron-Cohen et al., 2011). With the exception of Asperger’s syndrome, ASD frequently co-occurs with intellectual disability (Baird et al., 2006) and/or epilepsy (Woolfenden et al., 2012). As the prevalence of people diagnosed with ASD rises (Rutter, 2005), it becomes more and more imperative for healthcare workers in any setting, including family care, institutions, primary or acute care, to understand the unique challenges of this population.

The life expectancy of people with ASD is of interest to parents, health professionals and service providers concerned with these peoples’ lifetime needs. Monitoring survival in people with ASD is important not only to evaluate services and make projections for future resource allocation, but also to target inequalities and enable planning of services for disadvantaged groups of individuals within the population with ASD.

Occasional deaths have been reported in many follow-up studies of people with ASD (Fombonne et al., 1989; Kobayashi et al., 1992; Ballaban-Gil et al., 1996; Larsen and Mouridsen, 1997; Howlin et al., 2004; Billstedt et al., 2005; Eaves and Ho, 2008; Mordre et al., 2012). Systematic studies dealing with mortality and factors associated with death in ASD are rare. There are difficulties in obtaining sufficient sample sizes for the calculation of cause specific risks and the influence of age. There is also difficulty tracing all participants for a sufficient time and in establishing the factors associated with mortality. The studies published so far are limited to younger age groups, prohibiting the calculation of risks for older age groups of people with ASD. The aims of this review article are to increase the attention to mortality and to identify the most important factors associated with death in people with ASD. In the following sections I elaborate on current research on mortality in ASD. The identification of ill health and interventions to reduce avoidable mortality are given particular attention.

2. Standardized mortality ratio (SMR)

SMR is frequently used to describe excessive mortality. The SMR is the quotient of the observed to the expected numbers of deaths. An SMR of 1 indicates that the observed number of deaths is not different from what would be predicted for the general population, while an SMR value greater than 1 indicates that the observed mortality exceeds expectations in the group under study.

To my knowledge, only three systematic follow-up studies specifically dealing with mortality and causes of death in individuals with ASD have been published so far. Shavelle et al. (2001) reported mortality and causes of death in 13,111 young ambulatory Californians with ASD who received services from the California Department of Developmental Services between 1983 and 1997. The overall SMR was 2.4. When Pickett et al. (2006) updated the Shavelle et al. (2001) study and analyzed data for a more recent 5-year span, 1998-2002, the overall SMR for this period was 2.6. Comparable results were obtained in a Danish study (Mouridsen et al., 2008), in which an overall SMR of 1.9 was reported in a clinical cohort of 341 individuals with ASD followed between 1960-2007 with an average 43 years of age on the day of census. In a Swedish community study encompassing 120 people with ASD with a mean age of 33.2 years Gillberg et al. (2010) found an overall SMR of 5.6. The authors attributed this particularly high SMR to the use of a population based, rather than clinical, sample. When Woolfenden et al. (2012) combined the three aforementioned studies (Pickett et al., 2006; Mouridsen et al., 2008; Gillberg et al., 2010), the resultant pooled SMR was 2.8. This means that the expected number of deaths among the pooled
population with ASD is nearly three times higher than that among people of the same age and sex in the general population.

3. Risk factors for mortality

It is important to investigate specific factors associated with death in people with ASD in order to determine whether the deaths are potentially preventable. Cause-specific mortality rates offer baseline information for health promotion and are important for preventive strategies. When Woolfenden et al. (2012) summarized risk factors associated with mortality in their systematic review they emphasized that the risk factors identified for increased risk of mortality were heterogeneous and reflected the wide range of factors associated with mortality in the general population. The authors identified the following three risk factors to be most important.

3.1 Female gender

All three aforementioned studies reporting SMR found an increased risk of death associated with female gender. In the Sahavelle et al. (2001) study the SMR for males was 1.7 and 5.5 for females. Analyses by gender in the Mouridsen et al. (2008) study revealed figures of 1.6 and 4.0, respectively. Finally, Gillberg et al. (2010) reported an SMR of 2.3 for males and 20.7 for females. When SMR for males and females were pooled, the resultant SMR was 2.1 for males and 7.2 for females (Woolfenden et al., 2012).

3.2 Intellectual disability

Several authors have reported that degree of intellectual disability is associated with death risk in people with ASD. In the Sahavelle et al. (2001) study the SMR for participants with no or only mild intellectual disability was 1.4, compared with 3.1 for those with moderate to profound intellectual disability. Similarly, Gillberg et al. (2010) found that 8 of 9 deceased persons had a severe intellectual disability. In contrast, Mouridsen et al. (2008) found no significant difference between the two intellectual disability categories with respect to mortality risk: 8.4% against 7.1% (p = 0.7) had died by the close of the study.

3.3 Epilepsy

Shavelle et al. (2001) reported that the presence of seizures was associated with an SMR of 36.9 for those with a moderate to profound intellectual disability. This was in contrast to an SMR of 22.6 for those with no or mild intellectual disability only, suggesting that epilepsy increases mortality risk when there is also a severe intellectual disability. Mouridsen et al. (2008) found an SMR of 35.0 associated with epilepsy. Of the twenty-six deaths, eight (31%) were associated with epilepsy, judged as causal in four deaths. Gillberg et al. (2010) also reported that those who had died were more likely to have a co-occurring medical disorder, including epilepsy.

An association between ASD and epilepsy has been consistently reported and the literature presents a wide range of estimates from 5% to 46% (Spence and Schneider, 2009). These authors also reported that more severe intellectual disability resulted in elevated rates of epilepsy. These findings suggest that epilepsy should be considered in all individuals with ASD and a co-occurring intellectual disability. However, the clinical identification of seizures may be difficult in some cases, especially partial complex seizures, which can be largely complicated by the presence of atypical body movements and behavioural patterns often seen in association with ASD (Bauman, 2010). Obtaining a high quality EEG can be difficult and effective communication usually has to be through
a caregiver. Understanding of the needs of this group is particularly important within any epilepsy service. Since epilepsy is associated with reduced life expectancy, careful monitoring of antiepileptic treatment is essential in those individuals with ASD and a co-occurring epileptic disorder. The presence of ASD and/or intellectual disability complicates the management of epilepsy in regards to medication tolerability and adherence to medication management (Despositario-Cabacar and Zelleke, 2010). Complicating this further is the need for regular serum laboratory monitoring for some of the most potent anticonvulsant medications, which can be challenging to obtain in people with ASD and a co-occurring severe intellectual disability.

3.4 Accidents
A number of authors have reported elevated mortality of people with ASD related to accidents or other violent circumstances. In the study of Shavelle et al. (2001) suffocation and drowning was particularly common in younger individuals and among those with a moderate to profound intellectual disability; SMR = 51.4 and 13.7, respectively. For those with no or mild intellectual disability, the respective SMR values are 5.7 and 3.9. Mouridsen et al. (2008) found that three of twenty-six of ASD deaths were due to accidents (suffocation and drowning). Gillberg et al. (2010) reported that two of nine ASD deaths were due to accidents (drowning and poisoning). One of the three deaths in the study of Ballaban–Gil et al. (1996) followed drowning. Two of the six deaths in the autopsy study of Bauman and Kemper (1994) were also caused by drowning. Different kinds of accidents have been reported in other studies too. In the Fombonne et al. (1989) study, three people with ASD died from road accidents. One of the two reported deaths in the study by Larsen and Mouridsen (1997) was also caused by a traffic accident. Additionally, Kobayashi et al. (1992) reported that head injury resulting from self-injurious behaviour contributed to one of four deaths.

3.5 Infectious diseases
It has been reported that infectious diseases are contributing to excess deaths in populations with intellectual disabilities (Patja et al., 2001). In the Shavelle et al. (2001) study respiratory diseases (primarily pneumonia) were common diseases associated with death in the ASD group with a severe to profound intellectual disability, SMR=10.8. This was in contrast to an SMR of 1.3 in the ASD group with no or a mild intellectual disability only. In the Mouridsen et al. (2008) study infectious diseases were listed as a contributing factor in seven (27%) of the twenty-six ASD deaths. Eaves and Ho (2008) reported that cause of death was complications of a massive infection in a patient with ASD who had a co-occurring intellectual disability, and was on medication for both seizure disorder and depression. One of the three ASD deaths in the Ballaban-Gil et al. (1996) study was due to pneumonia; another death was due to complications arising from long-term psychotropic medication. In general, the many cases of death related to infectious diseases, points to the need for improved health promotion and health surveillance for this vulnerable group of people. Additionally, it is important to note that there appears to be a distinct subset of people with ASD with a history suggestive of frequent infections (Jyonouchi et al., 2008). In this distinct subset of people with ASD caregivers may continuously need to actively monitor risk of infection, in lieu of the communication deficits in moderate to severely affected individuals.

4. Preventive measures to reduce cases of avoidable deaths
Overall, preventive measures to decrease mortality in people with ASD should focus on those areas where death is potentially avoidable, such as infectious diseases and accidental deaths. However, it is worth nothing that the symptoms that characterize ASD (deficits in the areas of communication
and social skills) interfere with the correct diagnosis of illnesses. Furthermore, resistance to receiving medical care and possible sensory abnormalities to pain (Leekam et al., 2007) can make medical care difficult and in some cases result in exacerbations of somatic illness or diagnostic delay, eventually leading to deathly illness. In most of the reported studies insufficient information is available to identify preventable causes of death, or deaths which might have been due to suboptimal care. This might have to do with confidentiality issues or bias related to conduct root cause analysis. Nevertheless, this inhibits the ability to suggest appropriate interventions, although one could surmise that the high number of deaths related to infectious diseases may reflect too low a threshold for primary care involvement in managing intercurrent infections. Future studies should focus on providing more information regarding events surrounding death and report the causes of severe safety incidents and actions necessary to prevent its recurrence.

4.1 Increased preventive care

Larsen and Mouridsen (1997) reported a case of overlooked volvulus leading to death in a woman who lived in a long-term psychiatric institution. A similar course was reported in a study by Mouridsen et al. (2008), where a 24-year-old woman with ASD and co-occurring severe intellectual disability and epilepsy, who lived in a residential institution for people with an ASD, died due to meningitis purulenta. In this case the examining doctor initially erroneously misread the presenting symptoms as influenza. These cases highlight the importance of educating health practitioners about special considerations when diagnosing and treating people with ASD.

Although parents and caregivers of people with ASD might be aware of the increased mortality risk, it may be difficult for them to quickly detect the severity of an illness in people whose disability is characterized by a decreased ability to communicate and interact socially, and in some cases result in the provision of erroneous treatment (Smith et al., 2012). Heightened awareness, detailed histories, and a lower threshold to conduct a thorough examination and laboratory testing may be necessary in this vulnerable group of patients, combined with regular review of their well-being. The simple task of assessing pain and discomfort in a cognitively impaired, nonverbal patient is difficult. The best pain assessment by proxy is that provided by caregivers or family members who know the patient well. Only they can identify changes from a patient’s baseline behaviour that may signify pain and discomfort. People with ASD often find the experience of going into a medical setting frightening because of their inability to cope with a change in their routine and the problems in comprehending what is happening to and around them. Sensory overload from noise, smells, lights and crowded busy waiting rooms could exacerbate their behaviour problems (Olivie, 2012). Emergency rooms may be particularly anxiety provoking because of the sudden nature of the clinical event, the unpredictable waiting time on arriving and the number of people providing physical contact. In some people with ASD conventional peri- and postoperative management is impossible (Van Der Walt and Moran, 2001; Dell et al., 2008). Likewise, blood sampling, intravenous insertions, and initiation or change of medical treatment can be difficult to carry through (Davit et al., 2011). Noteworthy is that Williams et al. (2000) found that 62% of parents reported difficulty in giving medicine to their children with ASD.

4.2 Increased supervision for people with ASD

Since accidents are avoidable in most cases, special attention should be paid to safety of community surroundings (Mcllwain and Fournier, 2011). In this vein, Anderson et al. (2012) found that 48% of children with ASD had attempted to elope from a safe environment, a rate nearly four times higher than their unaffected siblings. Elopement/wandering risk was associated with autism severity. Of
those who were missing, 24% were in danger of drowning and 65% were in danger of traffic injury, suggesting that addressing elopement behavior is an important aspect of intervention for many people with ASD. In a study by Mouridsen et al. (2008), two participants, who for many years had lived in specialized institutions for people with an ASD, managed to swallow dangerous objects and choke on them during an unsupervised period of time. According to the standards of the caregivers the two patients should never be left alone. These examples of accidents illustrate the importance of maintaining a high standard of care of people with ASD, and emphasize that it is important to have organizational procedures making it possible for states or local authorities to review staff knowledge and competence on a regular basis. Other ideas include the development of best practice nursing standards that addresses care for people with ASD. Ultimately, the best plan of care will be one that is formulated with the family and considers the unique experience of the spectrum of individual's symptoms. With new insight into the excess mortality and common factors associated with death among people with ASD, there is now a greater ability to evaluate preventive measures and medical care practice that may ensure the well being of these individuals.

5. Conclusion

A person with ASD is predisposed to different physiological and environmental risks, which produce disparities in mortality patterns, leading to different life expectancy. The evidence to date suggests that the all-cause observed number of deaths is nearly three times higher in populations with ASD than in the general population. Females, and those with a moderate to profound intellectual disability or who have co-occurring epilepsy have a larger reduction in life expectancy. If we intend to reduce the avoidable mortality in people with ASD, then we need to focus especially on risks of accidents and preventing infectious diseases. Therefore, well-coordinated care among the individual’s primary caregiver, internist and neurologist is essential to minimize mortality, and optimize health and quality of life.

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