Annals of Epidemiology 25 (2015) 236–242

Contents lists available at ScienceDirect

Annals of Epidemiology

journal homepage: www.annalsofepidemiology.org

Original article

A population-based prospective birth cohort study of childhood neurocognitive and psychological functioning in healthy survivors of early life meningitis

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ARTICLE INFO

Article history:
Received 18 January 2014
Accepted 5 November 2014
Available online 20 November 2014

Keywords:
Meningitis
Central nervous system infections
Intelligence
Memory
Educational achievement
Affective symptoms
Behavioral problems
Psychotic experience
Depression
Anxiety
Psychosis

ABSTRACT

Purpose: To determine neurocognitive, educational, and psychological functioning during childhood and early adolescence among survivors of early life meningitis who are apparently healthy.
Methods: In the general population-based Avon Longitudinal Study of Parents and Children birth cohort, meningitis exposure was determined at age of 18 months. The outcomes of intelligence quotient, short-term memory, working memory, reading and spelling abilities, psychological and behavioral problems, depressive and anxiety symptoms, and psychotic experiences at ages 9 to 13 years were compared between those exposed and unexposed to meningitis. Individuals with special educational needs were excluded.
Results: By age of 18 months, 67 of 11,035 children were reported to have suffered from meningitis (0.61%). These children, compared with the unexposed, performed worse on all neurocognitive and educational measures; mean difference in total intelligence quotient 7.36 (95% confidence interval, 1.60–13.11). Meningitis was associated with higher depressive and anxiety symptoms ($P = .02$), psychological and behavioral problems ($P = .09$), and increased risk of psychotic experiences; risk ratio 2.22 (95% confidence interval, 1.12–4.38).
Conclusions: Exposure to meningitis in the early life is associated with neurocognitive, educational, and psychological difficulties during childhood and early adolescence among survivors who are apparently healthy. Therefore, focusing only on serious neurologic disabilities may underestimate the true impact of early life meningitis.

Introduction

Meningitis is inflammation of the membranes (meninges) that surrounds and protects the brain and spinal cord. It is most often caused by an infection (bacterial, viral, or fungal) but can also result from noninfectious causes [1–3]. Meningitis is associated with considerable death and disability: yearly an estimated 171,000 deaths and 9.8 million disability-adjusted life years worldwide according to the World Health Organization (WHO) [4]. Early life meningitis, particularly during the neonatal period, is associated with high mortality and morbidity [5–8].

Major sequelae of childhood meningitis have been studied extensively, which in case of bacterial meningitis includes permanent neurologic disability, sensory and motor impairment, intellectual disability, or loss of a limb [9–14]. However, with improved antimicrobial therapy, serious complications from early life meningitis are increasingly less common in the Western countries [13]. According to a recent systematic review and meta-analysis of global data on childhood bacterial meningitis, the risk of at least one major sequela is 9% in the WHO European region compared with over 20% in Africa and South Asia [13]. Although relatively less studied,

The authors have no conflicts of interest to disclose.

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http://dx.doi.org/10.1016/j.annepidem.2014.11.013
1047-2797/

meningitis is associated with poorer neurocognitive and educational performance. Studies have reported deficits in intelligence quotient (IQ), memory, increased emotional symptoms during childhood, and adolescence among survivors of early life meningitis [10–12,15,16]. This suggests serious complications, which are often used to measure the impact of childhood meningitis, may only represent the tip of the iceberg in terms of disability associated with the illness.

Previous studies have commonly included meningitis survivors with or without serious complications as a single group, but there is evidence that cognitive impairments are greater in those with a neurologic disability, such as hearing impairment, than those without [11]. Thus, the true burden of neurocognitive and psychological difficulties in meningitis survivors who are apparently neurologically healthy remains to be determined. Many studies have used short follow-up; tests administered at the time of discharge from hospital may not reflect long-term neurocognitive performance [13]. Therefore, studies with long duration of follow-up based on representative general population samples are necessary to accurately measure the associations between early life meningitis and long-term neurocognitive abilities.

To determine long-term functioning in survivors of early life meningitis who are apparently healthy, we have carried out a 12-year follow-up study of meningitis occurring in the first 18 months of life in the Avon Longitudinal Study of Parents and Children (ALSPAC), a general population birth cohort. Focusing exclusively on individuals without a serious neurologic disability, we have compared neurocognitive and educational performance assessed as IQ, short-term memory, working memory, reading and spelling abilities between ages 9 and 11 years, psychological and behavioral problems at age 10 years, symptoms of depression and anxiety at age 11 years, and risk of developing psychotic experiences (PEs) at age 13 years between those exposed and unexposed to meningitis. We predicted that early life meningitis will be associated with poorer performance in neurocognitive, educational, and psychological tasks during childhood and early adolescence.

Methods

Ethical approval

Ethical approval for the study was obtained from ALSPAC Ethics and Law Committee and the Local Research Ethics Committees. Parents of all participants provided informed written consent.

Description of cohort

The ALSPAC birth cohort is based on all pregnant women resident in the county of Avon, a geographically defined region in the southwest of England, with expected dates of delivery between April 1991 and December 1992 (www.alspac.bris.ac.uk). The initial ALSPAC cohort consisted of 14,062 live births and 13,988 infants still alive at 12 months [17,18]. Avon included both urban and rural areas, and the population was broadly representative of all children in the United Kingdom. The parents completed regular postal questionnaires about all aspects of their child's health and development since birth. Since the age of 7 years, the children attended an annual assessment clinic during which they participated in a range of face-to-face interviews and physical tests.

The present study is based on 11,035 participants whose parents provided data on meningitis when the study child was on average 18.3 months old. The number of individuals with available information for both meningitis and specific outcome measures vary as the latter were completed by different number of individuals (Fig. 1). At age of 9 years, information on special educational needs were gathered by trained interviewers for the entire cohort that identified 63 children with special needs (20 learning disabilities, 11 attention deficit hyperactivity disorder, eight dyslexia, seven visual or hearing impairments, and 17 with motor or other impairments). None of these children was reported by their parents to be exposed to meningitis. Children with special educational needs were excluded from analyses to improve comparability between exposed and unexposed groups, that is, meningitis-exposed children without special educational needs were compared with meningitis-unexposed children without special educational needs.

Assessment of meningitis

Data on exposure to meningitis were gathered using a questionnaire completed by parents when the ALSPAC participants were on average 18.3 months old. Parents were asked whether the child suffered from meningitis anytime since birth. They could respond either "yes" or "no," which was used to determine whether the child suffered from meningitis in the first 18 months of life. At the time of reporting, the age range of the child was 18 to 31 months; however, 95.8% of the children were 18 or 19 months old.

Assessment of neurocognitive and educational performance

General intelligence and short-term memory (average age, 9 years)

IQ was measured by the Wechsler Intelligence Scale for Children (WISC III, third UK edition) [19]. A shortened version of the test was applied by trained psychologists, whereby only alternate items were used for all subtests with the exception of the coding subtest which was administered in its standard form. Digit span subtest of WISC III was used as a measure of short-term memory. The WISC has been reported to have very good internal consistency and inter-rater reliability. Inter-rater reliability coefficients for verbal, performance, and full scale IQ are all greater than 0.9, which is excellent [20,21].

Reading and spelling abilities (average age, 10 years)

Two reading tasks and a spelling task were administered by trained psychologists and speech therapists. Reading was assessed by asking the child to read out loud 10 real words, followed by 10 nonwords. The tester recorded whether the child read each word correctly or incorrectly or whether the child did not attempt the task. For the spelling task, the child was given a series of 15 words to spell. For each word, the tester first read the word out loud on its own to the child, then within a specific sentence incorporating the word and finally alone again. The child was asked to write down the spelling of the word even if she or he thought they were just guessing. The tester recorded whether the child got each spelling correct or incorrect or whether the child did not attempt the task. The two sets of words for the reading tasks and one set of words for the spelling task were specifically chosen for use in ALSPAC after consulting the developers of these tasks [22]. Final score for each task was used. These tasks have good validity and reliability for assessing reading and spelling abilities in children. The test–retest reliability coefficient for the word reading task is 0.80. It has a correlation of 0.85 with the Schonell Word Reading Task, and 0.81 with the word spelling given 4 months later [23].

Working memory (average age, 11 years)

Computerized Counting Span Task was used [24], which tests information processing and storage abilities simultaneously. A child's working memory span was calculated automatically by the computer program. The maximum score a child could achieve was five (i.e., all correct). We used the span score, which is the main outcome measure from this task.