Does otitis media in early childhood affect later behavioural development? Results from the Western Australian Pregnancy Cohort (Raine) Study

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Abbreviations: Otitis Media (OM), rOM (Recurrent Otitis Media), Child Behaviour Checklist (CBCL)

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Abstract

Objectives: To examine the relationship between early life episodes of otitis media and later behavioural development with adjustment for confounders.

Design: Longitudinal cohort study.

Setting: The Western Australian Pregnancy Cohort (Raine) Study recruited 2900 pregnant women from King Edward Memorial Hospital (KEMH) in Perth, Western Australia, between 1989 and 1991.

Participants: Data from the children born were collected at both the Year 3 and Year 5 follow up. At Year 3, $n = 611$ were diagnosed with recurrent otitis media through parent-report and clinical examination. At Year 5, $n = 299$ were considered exposed to otitis media based upon tympanometry results.

Main Outcome Measures: Performance in the Child Behaviour Checklist (CBCL), a questionnaire completed by the primary caregiver at Year 10.

Results: Significant associations were found between recurrent otitis media at Year 3 and internalising behaviours ($P = 0.011$), and the somatic ($P = 0.011$), withdrawn ($P = 0.014$), attention ($P = 0.003$) and thought problems domains ($P = 0.021$), and the total CBCL score ($P = 0.010$). A significant association was also found between exposure to otitis media at Year 5 and externalising behaviours ($P = 0.026$).

Conclusions: A modest association was seen between recurrent otitis media at Year 3 and exposure to otitis media at Year 5 and a number of behaviour domains at Year 10.

Introduction

Otitis media (OM) is a general term used to describe conditions that involve the inflammation of the middle ear cleft and is highly prevalent in early childhood, affecting up to 90% of children prior to school entry.[1,2] Effusion associated with OM and the resultant hearing deficit has been shown to compromise language development, which can, in turn, influence the behaviour of affected children.[3] However, behavioural development is a multifactorial process. Therefore it has been difficult to establish a direct association between OM and poor behavioural development, without the influence of confounding factors. The aim of this longitudinal investigation was to examine the relationship between early life episodes of OM and poor behavioural development with adjustment for potential prenatal, postnatal and environmental confounders. The underlying hypothesis was that the presence of OM would influence the development of behavioural problems in later childhood, including a higher prevalence of conduct problems, hyperactivity and attention difficulties.[3-5]

It should be noted that previous studies in this area have been restricted in their application to clinical practice due to a number of design limitations, including small sample size,[6,7] purely subjective detection of OM,[3,8] selection bias,[4,9] and the presence of multiple confounding factors.[8,10-13] This study sought to address these limitations, with the intention of producing findings to better inform our approach to management and intervention for children with OM.

Methods

Ethical Considerations

Human ethics committees at both King Edward Memorial Hospital (KEMH) and Princess Margaret Hospital in Perth, Western Australia, approved participant recruitment and follow-up for the Western Australian Pregnancy Cohort (Raine) Study. Informed written consent was obtained from every pregnant woman and consent was also obtained at each follow up stage from the guardian of each child participant. Each child participant was then re-consented at age 18 years for the use of stored data. All data provided was de-identified prior to receipt.

Raine Study Participants

This study is based on data from the Raine Study, a longitudinal cohort study of 2900 pregnant women who volunteered to be a part of a study at KEMH, the sole tertiary maternity hospital in Western Australia. These women were recruited from various private and public hospitals within Perth, Western Australia, between the months of May 1989 and November 1991.[14] To be eligible for participation, these women were required to have a gestational age between 16 and 20 weeks, proficiency in English language sufficient enough to understand the implications of participation, the expectation to deliver their baby at KEMH, and the intention to continue residency within Western Australia.[14] The 2868 live born children from these pregnancies have been assessed over the past 28 years with respect to a number of factors. These included middle ear pathology,[2,15] and behavioural characteristics.[2,16]

Variables

Diagnostic Criteria

The presence of OM in the Raine Study was identified through a number of different methods. Two sample populations were selected based upon different identification

criteria, each with their own strengths and limitations. The first sample included those children within the Raine Study cohort that had a recurrent history of OM (rOM) at the Year 3 follow-up, when children were approximately three years of age.[2] These children were identified by a positive answer to the question, 'has your child ever in his/her life [had] otitis media (middle ear infection)? If so, how many?' If a participant was reported as having three or more episodes of OM in the first three years of life, they were considered to have a diagnosis of rOM.[2] If clinical examination by a specialist nurse revealed scarred, retracted, inflamed or perforated tympanic membranes, the presence of middle ear effusion or ventilation tubes in situ during the Year 1 – Year 3 follow-ups, they were also said to have a diagnosis of OM and included in this sample population,[2] ($n = 611$).

The second sample included those children that underwent a otoscopic examination with tympanometry at the Year 5 follow-up assessment, when children were approximately six years of age[15,17] the earliest time point in which this type of assessment was completed in this cohort. Type B tympanograms provide a measure of the presence of middle ear effusion, which was used to indicate exposure to OM (either acute OM or OM with effusion).[15] Either unilateral or bilateral Type B tympanograms were included in this cohort ($n = 299$). Note that a definitive diagnosis of OM cannot be made using cross sectional data.

Outcome Measure

The outcome measure for this study was the Child Behaviour Checklist (CBCL) score, an empirically validated measure of child behaviour for use in children aged 4-18 years. This was completed by the primary caregiver at the Year 10 follow-up, when participants were approximately 10 years of age.[16] The CBCL is a commonly used dimensional rating scale for emotional and behaviour problems in children that

has been shown to be a good predictor of functional and behavioural impairment later in life,[16] with good internal reliability and validity across a range of populations.[16] The CBCL is a questionnaire consisting of 118 questions that are based on specific problem behaviours that may have been observed in the past 6 months. It is scored using a 3-point Likert Scale where 0 indicates the behaviour is absent; 1 indicates that the behaviour occurs sometimes; and 2 indicates that it occurs often.[18] Performance in the CBCL is calculated using a total t-score (standardised by age and gender), with results apportioned across a number of relevant behavioural domains including withdrawn, somatic complaints (such as abdominal pain), anxious/depressed, social problems, thought problems, attention problems, delinquent behaviour, and aggressive behaviour. Some of these domains are also summarised under two behavioural subscales, internalising behaviours (problems within oneself) that include the somatic, withdrawal and anxious depressed domains, and externalising behaviours (conflicts with others or against societal expectations) that include the delinquency and aggression domains. Note that the t-scores, as opposed to raw scores, were used in this analysis.

Potential Confounders

In order to minimise confounding bias, a number of potential risk factors for OM, identified through the literature, were accounted for in the analyses.[2] These risk factors are listed in Tables 1 and 2.

Statistical Methods

The prevalence of the predicted risk factors within both the rOM in the Year 3, and exposure to OM in the Year 5, sample populations was determined using frequency distributions (See Tables 1 and 2). Multiple linear regression models were then used to compare the continuous CBCL data across a number of domains at Year 10 as the

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dependent variable, against all the possible risk factors, alongside rOM at Year 3 and exposure to OM at Year 5 as the independent variables (See Tables 3 and 4). For all analyses, $p < 0.05$ was considered statistically significant. Data was analysed using IBM SPSS Statistics for Macintosh, Version 23.0 (Armonk, NY: IBM Corp).

Results

The overall prevalence of rOM at Year 3 was 26.8% (611/2277), and 22.3% (299/1343) for exposure to OM at Year 5. Of those with a rOM at Year 3, 85.4% (522/611) had CBCL data recorded at Year 10, and of those exposed to OM at Year 5, 88.6% (265/299) had CBCL data recorded at Year 10. Of those without rOM at Year 3, 81.6% (1349/1666) had CBCL data recorded at Year 10, and of those that were not exposed to OM at Year 5, 89.6% (935/1044) had CBCL data recorded at Year 10. A comprehensive range of potential risk factors for OM were available in the Raine Study and the prevalence of these within both Year 3 and Year 5 sample populations are displayed in Tables 1 and 2 respectively.

When using multiple linear regression analyses to estimate the predicted change in CBCL scores associated with the presence of rOM at Year 3, it was found that there was a statistically significant association between rOM at Year 3 and internalising behaviours, the somatic complaints domain, the withdrawn domain, the attention problems domain, and the thought problems domain of CBCL scores, as well as the total CBCL score, after controlling for the effects of all other predictors in the model (Table 3).

When using multiple linear regression analyses to estimate the predicted change in CBCL scores associated with exposure to OM at Year 5, it was found that there was a statistically significant association between the exposure to OM at Year 5 and

externalising behaviours after controlling for the effects of all other predictors in the model (Table 4).

Discussion

The analysis demonstrates a modest association between early life episodes of OM and behavioural development in later childhood as determined through CBCL data, a standardised measure of behaviour. The association differs between each group with rOM at Year 3 being associated with a greater range of behavioural problems measured at Year 10 in comparison with exposure to OM at Year 5. This may be a reflection of the nature of OM identification in this population, as those children with recurrent episodes of OM over a three-year period were selected, as opposed to the Year 5 recruitment cohort, which was cross-sectional. Recurrent OM is more strongly associated with an extended loss of hearing sensitivity, which is more likely to lead to problematic behaviour such as hyperactivity and attention deficit.[2,3,19] Parental reporting is also more likely to capture the presence of more serious disease, as parents are more likely to recall events of greater chronicity and severity.[3] Furthermore, as the data were collected at a younger age, episodes of OM in this sample population are more likely to be captured during the critical period of language development, which is said to be during the first few years of life.[13,19,20] If hearing is disrupted during this critical period, the cognitive areas associated with auditory processing, speech and language may be affected, resulting in a greater chance of developing the behavioural problems observed due to the inability to communicate effectively.

Though exposure to OM at Year 5 was determined through a more objective means in comparison with parental report,[21] it does not provide clear information with respect to either the severity or time course of the condition. This is because the data itself is

based upon a single point in time. Though the presence of effusion can be indicative of chronicity, with the average duration of OM with middle ear effusion said to be three months and likely to recur,[21] this cannot be said for certain within this population without trajectory analysis. This method of diagnosis is also at risk of under diagnosing the prevalence of OM in this population, which may underestimate the extent of any effects seen. Nevertheless, the results still demonstrate a significant association with externalising behaviours overall indicating that exposure of OM, irrespective of whether the exposure is prolonged, is still a sensitive variable. This is in line with studies that state that the severity and duration of episodes of OM are inconsequential to the development of behavioural sequelae,[22] though it may contribute to the severity of the deficit seen.

It was interesting to note that rOM at Year 3 was associated with internalising behaviours, whereas exposure to OM at Year 5 was associated with externalising behaviours. It is suggested that the development of externalising behaviours is more strongly associated with a hearing deficit, whereas internalising behaviours is more strongly associated with chronic disease of any causation.[3] This can be related back to the results obtained as the presence of OM is associated with an average hearing loss of between 20 and 30 decibels (dB).[21] As such, identification through tympanometry may have captured more participants with a confirmed hearing deficit compared with parental report. This may have contributed to the association with externalising behaviours observed. In addition, rOM is related to recurrent episodes of OM, a variable more strongly associated with chronic disease. As a result, these children with recurrent OM may have been more likely to develop internalising behaviours later in life. Nevertheless, it is thought that such dichotomous terms for behaviour are actually misleading as a single individual can display both types of behaviour concurrently.[23,24] Therefore, the association with behavioural deficits as a whole was

considered for the purposes of this study, rather than a focus on specific behavioural domains.

Strengths and Limitations

This investigation was embedded within the Raine Study, which enabled the inclusion of a large and prospectively studied participant cohort. The wealth of data collected has ensured that a wide range of potential risk factors associated with the development of OM could be identified and accounted for within the analysis. This helped determine the extent to which OM was associated with behaviour without the influence of confounders.[8,10-13] Similarly, the use of the Raine Study data has allowed for a larger, population-based sample size to be analysed, increasing the external validity of the data. Another strength of this study is the use of CBCL to identify behavioural deficits. The CBCL has demonstrated strong internal consistency in the identification of psychopathology in children, and is also deemed comparable with other studies that describe behavioural deficits in childhood.[16] Although there is the potential for observer bias as CBCL data is based upon parental perspective of behaviour, which could be affected by the circumstances of the individual parent,[23] the use of this data as the primary outcome measure has been validated,[16] particularly for the prediction of child and adolescent mental health outcomes.[18]

A number of limitations in this study should also be considered when interpreting the results. Though many risk factors were identified and accounted for in the multiple linear regression models, not all risk factors could be included due to a lack of data. For example, a family history of OM, pacifier use, upper respiratory tract infection, and snoring have all been linked with the development of OM across a wide range of studies,[2] yet were not available through the Raine Study. The issues associated with the identification of OM were also an important limitation, in particular the potential

for recall bias through the use of parental report. Despite this possibility, it should be noted that the sensitivity and specificity of rOM has been calculated as between 75-95% and 65-100% respectively,[25] with parents more likely to underestimate the number of episodes a child has experienced.[2] The ideal method would be for all those children identified to be subject to clinical confirmation with either tympanometry or pneumatic otoscopy, and continuous monitoring over a set time period to determine the extent and chronicity of the disease.[2] However, the resources required to achieve this were not available in this study.

Conclusions

This study has shown that a modest association exists between rOM at Year 3 and exposure to OM at Year 5 and several behavioural domains in later childhood, when controlling for confounders. Though this association is minor across all domains, it is interesting to note that an association with behaviour still exists with respect to OM, between 5 to 7 years after the condition was first recorded. These associations are often diminished over time due to the natural accumulation of other sources of variance.[3] As the presence of behavioural issues in childhood has a strong influence upon later mental health outcomes, this finding could create a target population for the monitoring of key language milestones and subsequent early intervention if deficits become apparent.[16,19,24]

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CONFLICT OF INTEREST

None to declare.

Table 1: Characteristics of the study population by presence of rOM at Year 3

Risk Factors	rOM at Year 3 (*n*=611)		No rOM (*n*=1666)	
	n	*%*	*n*	*%*
Male Gender				
Yes	327	53.5	827	49.6
No	284	46.5	839	50.4
Mother Spoke Language Other than English				
Yes	23	3.8	100	6.0
No	588	96.2	1566	94.0
Maternal Ethnicity				
Caucasian	585	95.7	1462	87.8
Other	26	4.3	204	12.2
Household Income Below Poverty Line				
< AU$24,000 per annum	225	36.8	636	38.2
> AU$24,000 per annum	361	63.2	952	61.8
Low Maternal Education				
< Year 12	343	56.1	945	56.7
> Year 12	254	43.9	686	43.3
Passive Smoking				
Yes	215	35.2	562	33.7
No	316	64.8	839	66.3
Parity				
No older siblings	256	41.9	836	50.2
One or more older siblings	355	58.1	829	49.8
Prematurity (< 37 week gestation)				
Yes	47	7.7	143	8.6
No	552	92.3	1483	91.4
Breastfeeding Stopped				
< 6 months	294	48.1	702	42.1
> 6 months	285	51.9	837	57.9
Low birth weight (< 2500 g)				
Yes	48	7.9	144	8.6
No	561	92.1	1517	91.4
Alcohol in Pregnancy (at 34 week gestation)				
Once a week or more	252	41.2	574	34.5
Zero Alcohol	319	58.8	960	65.5
Daycare Attendance				
Yes	346	56.6	739	44.4
No	99	43.4	375	55.6
Introduction of Other Milk				
< 6 months	435	71.2	1087	65.2
> 6 months	142	28.8	441	34.8
Asthma				
Yes	95	15.5	195	11.7
No	516	84.5	1471	88.3
Allergies				
Yes	188	30.8	348	20.9
No	322	69.2	946	79.1

Table 2: Characteristics of the study population by exposure to OM at Year 5

Risk Factors	OM at Year 5 (*n*=299)		No OM (*n*=1044)	
	n	*%*	*n*	*%*
Male Gender				
Yes	136	45.5	471	45.1
No	163	54.5	570	54.6
Mother Spoke Language Other than English				
Yes	273	91.3	994	95.5
No	26	8.7	47	4.5
Maternal Ethnicity				
Caucasian	257	86.0	957	91.9
Other	42	14.0	84	8.1
Household Income Below Poverty Line				
< AU$24,000 per annum	114	38.1	370	35.5
> AU$24,000 per annum	171	57.2	625	64.5
Low Maternal Education				
< Year 12	159	53.2	574	55.1
> Year 12	133	44.5	451	44.9
Passive Smoking				
Yes	103	34.4	315	30.3
No	148	49.5	573	69.7
Parity				
No older siblings	142	47.5	455	43.7
One or more older siblings	156	52.2	586	56.3
Prematurity (< 37 weeks gestation)				
Yes	19	6.4	72	6.9
No	273	91.3	948	93.1
Breastfeeding Stopped < 6 months				
Yes	156	52.2	439	42.2
No	125	41.8	559	57.8
Low birth weight (< 2500 g)				
Yes	21	7.0	75	7.2
No	278	93.0	963	92.8
Alcohol in Pregnancy (at 34 week gestation)				
Once a week or more	105	35.1	399	38.3
Zero Alcohol	173	57.9	569	61.7
Daycare Attendance				
Yes	132	44.1	510	49.0
No	77	25.8	213	51.0
Introduction of Other Milk				
< 6 months	190	63.5	798	76.7
> 6 months	91	30.4	283	23.3
Asthma				
Yes	37	12.4	137	13.2
No	262	87.6	904	86.8
Allergies				
Yes	73	24.4	252	24.2
No	168	56.2	599	75.8

Table 3: Output of standard multiple regression analyses comparing the effect of rOM at Year 3 upon CBCL scores adjusting for all potential risk factors

	β	SE (β)	*P*	95% CI (β)	
Total Score	2.03	0.79	**0.010***	0.48	3.57
Internalising	1.84	0.72	**0.011***	0.42	3.26
Externalising	1.37	0.75	0.069	-0.11	2.84
Delinquent	0.32	0.45	0.472	-0.59	1.20
Anxious/Depressed	0.80	0.42	0.058	-0.03	1.62
Somatic	1.28	0.50	**0.011***	0.30	2.25
Withdrawn	0.96	0.39	**0.014***	0.20	1.72
Attention	1.38	0.46	**0.003***	0.48	2.28
Aggression	0.64	0.43	0.140	-0.21	1.49
Thought Problems	0.90	0.39	**0.021***	0.14	1.66
Social Problems	0.82	0.45	0.072	-0.07	1.70

Table 4: Output of standard multiple regression analyses comparing the effect of exposure to OM at Year 5 upon CBCL scores adjusting for all potential risk factors

	β	SE (β)	P	95% CI (β)	
Total Score	1.50	1.07	0.163	-0.61	3.60
Internalising	0.85	1.00	0.395	-1.12	2.82
Externalising	2.31	1.03	**0.026***	0.28	4.33
Delinquent	0.83	0.62	0.178	-0.38	2.04
Anxious/Depressed	0.53	0.57	0.353	-0.59	1.64
Somatic	-0.80	0.67	0.231	-2.12	0.51
Withdrawn	0.79	0.55	0.148	-0.28	1.86
Attention	-0.04	0.61	0.948	-1.23	1.15
Aggression	0.72	0.58	0.216	-0.42	1.86
Thought Problems	-0.08	0.52	0.876	-1.10	0.93
Social Problems	0.29	0.61	0.631	-0.90	1.48

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