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Ten years of evidence for the diagnostic assessment of preschoolers with prenatal alcohol exposure

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ABSTRACT

The assessment of preschoolers with prenatal alcohol exposure (PAE) is challenging for many diagnostic teams and clinicians. The 2016 Canadian Fetal Alcohol Spectrum Disorder (FASD) diagnostic guidelines describe the assessments recommended for individuals with PAE in various age groups. Interpretation of brain domains constituting global impairment in preschoolers is not well described in the literature, and there has been clinical reluctance to consider the interpretation of clinical assessments as definitively diagnostic in this age group. This study describes the results of 10-year retrospective clinical data of over 300 preschoolers with PAE referred to the Manitoba FASD Centre for assessment of FASD. Preschoolers who met the criteria for a diagnosis of FASD showed significantly greater global developmental impairment, compared with those with PAE alone. They also demonstrated poorer receptive and expressive language

abilities when compared with preschoolers who were not diagnosed. Preschoolers with FASD were rated as having more difficulties with executive functioning skills and adaptive functioning skills, compared to their counterparts. Significant deficits were found in fine-motor, visual-motor, and components of gross-motor skills. Importantly, significant sensory processing differences are particularly evident in preschoolers and are important in understanding behavior and in intervention planning. Together, standardized assessment of motor and sensory processing skills, with a comprehensive assessment of language, are significant predictors of FASD diagnosis for preschoolers with PAE.

Keywords: *Canadian; diagnostic assessment; Fetal Alcohol Spectrum Disorder (FASD); prenatal alcohol exposure; preschool child*

INTRODUCTION

Fetal Alcohol Spectrum Disorder (FASD), a diagnostic term, describes the physical and neurocognitive effects of prenatal alcohol exposure (PAE) (1). Although there is extensive research on school-age children and adolescents, there is a limited body of research describing the assessment of neurobehavioral patterns seen in preschoolers with PAE. While the impact of PAE on preschool developmental domains can be challenging to assess, quantifiable clinical changes have been observed, and research has shown that many of these changes worsen over time (2–4). Early intervention and diagnosis are important in reducing the effects of FASD on children and ameliorating developmental patterns as the children age. The assessment of preschoolers with PAE should be a priority to support understanding of the current behavior and development, identify needs for supportive services and therapies, and support positive long-term outcomes.

BACKGROUND

Clinicians are often asked to assess preschoolers with PAE with developmental delays and challenging behaviors; however, clinicians and researchers have expressed several concerns around diagnosing FASD in the preschool population. Concerns include risk determination based on PAE alone, neuroplasticity, and the potential for the developmental impacts of both ameliorating factors and postnatal risk factors. The sensitivity of preschool assessments to later functioning is often cited clinically. Clinicians may express concerns about determining risk based on the level of confirmation of PAE, and often central to these concerns is the discomfort of attributing multiple factors to PAE alone (5).

Diagnostic assessment of preschoolers with PAE should consider differences in brain development as well as the interpretation and availability of standardized assessment tools. Brain development of infants and preschoolers is typically highlighted by thinner cortical structures, reduced cortical volume, and reduced myelination of white matter (6, 7). PAE negatively impacts neuronal migration and its genetic signaling, with direct consequences on the development of gray and white matter integrity, as well as changes in neurochemistry and intrinsic networks of connectivity (8–11). The impact of these neurological changes influences multiple brain domains of functioning, including cognitive, adaptive, motor, language, and sensory processing, which also potentially impact the assessment of brain structure and growth (10, 11). Neuroplasticity and postnatal development may ameliorate some of

the negative effects of PAE. However, these studies suggest changes to neural formation as a result of PAE, which are apparent early in life, have a lasting impact, and may be sensitive indicators of that exposure (11). Therefore, clinicians should be attentive to children at risk based on PAE and refer them for early neurobehavioral assessment.

There are relevant concerns regarding preschool assessment practices required to describe the multiple brain domains defined in current guidelines, as well as in the attribution of difficulties to PAE (4, 12–14). In 2016, a Canadian updated set of guidelines were published to describe the multidisciplinary diagnosis of FASD, which acknowledged differences in preschool assessment while recognizing the limitations in existing evidence (1). The Canadian guidelines define both functional and structural brain domains to be assessed in the multidisciplinary diagnostic evaluation, including motor skills; neuroanatomy/neurophysiology; cognition; language; academic achievement; memory; attention; executive functioning, including impulse control and hyperactivity; affect regulation; and adaptive behavior, social skills, or social communication (1). An FASD diagnosis may be made when there is severe impairment (typically defined as below 2 standard deviations (SD) on standardized testing) in three or more of the neurodevelopmental domains in the presence of PAE and when other neurodevelopmental disorders are excluded (1).

The multidisciplinary diagnostic team examines sentinel facial features (SFF) and other dysmorphology, including microcephaly. Differential diagnosis is specifically considered and may include diagnostic explanations related to genetics or the social and environmental factors of the child. Young children may not meet FASD diagnostic criteria because the currently used tests may not be sensitive to these differences at young ages, including variability in learning profiles or subtler neurobehavioral problems individually, and because the team may attribute the children's difficulties to other explanations such as trauma or attachment difficulties (2).

Therefore, a diagnosis in preschool children is often deferred (15). A deferral often means that preschoolers and their families are not able to access early intervention and supports specific to PAE. Despite concerns about assessing neurodevelopment in preschoolers, some research has shown that children who have an FASD diagnosis display neurobehavioral impairments that are consistent with deficits found in older children and adolescents with FASD (4). Furthermore, the neurobehavioral impairments displayed by children with PAE often persist into adulthood, particularly in the absence of informed early intervention and supports (4). Taken together, these observations support early identification and comprehensive assessment of preschoolers with PAE to advocate for appropriate early intervention and thereby improve outcomes.

Hypothesis and Objectives

The purpose of this study is to provide clinical evidence for conducting diagnostic assessments of preschool children for FASD by identifying clinical predictive features that support early diagnosis of FASD and offering a clinically experienced interpretation from a multidisciplinary team over the last decade. The main objectives of this study are to: (1) describe data on preschool multidisciplinary assessment of preschool children with PAE seen through the Manitoba FASD Centre between 2005 and 2016; (2) describe characteristics in the brain domains considered for an FASD diagnosis; (3) model predictive characteristics of FASD in preschoolers; and (4) propose improved clinical practices for the assessment of preschoolers with PAE.

METHODS

Design

This study is a retrospective chart review of 340 preschool assessment data on children aged 3–6 years seen at the Manitoba FASD Centre between

2005 and 2016. Children were assessed by a multidisciplinary team that consisted of a developmental pediatrician, geneticist, occupational therapist, speech-language pathologist, and psychologist.

Retrospective data from the multidisciplinary assessments of these children were collected, including demographic data, multidisciplinary assessment data (language, motor, sensory, behavioral, and developmental assessments), diagnostic data, and comorbidities. Some missing data on early assessments are present for different domains, as earlier assessments completed prior to the Canadian guidelines may have included different subtest combinations, resulting in slightly different total numbers. In the case of repeat assessments, the most recent data were used in this analysis, making 332 the total number of complete assessments.

Population

The study data came from children referred for assessment at the Manitoba FASD Centre and provincial network, which is the central diagnostic program serving the provincial population in Manitoba, Canada. It was established in 1999 and works with diagnostic coordinators throughout the province using a centralized coordinated model. The Manitoba FASD Centre has assessed over 4000 children since its inception, at a rate of approximately 200–240 assessments per year. Consistently since 2005, approximately 60% of the children seen at the Manitoba FASD Centre are in agency care, 30% are with birth families, and 10% have been adopted. The Manitoba FASD Centre has a screening and intake process, which carefully considers PAE, consent, the timing of the assessment, the social situation, and the neurodevelopmental difficulties. In this study, all children assessed had confirmed PAE in keeping with the recommendations of the Canadian diagnostic guidelines (1).

Preschoolers were diagnosed using Canadian diagnostic guideline nomenclature of FASD with or without SFF (1). In addition, all children received a 4-digit diagnostic code following Astley's extensively validated 4-digit code, first established with the Washington Diagnostic & Prevention Network in 1997, and currently released in 2004 with multiple validations published since (16, 17). This code describes the physical, facial, and neurocognitive features, and a measure of prenatal alcohol confirmation using a 4-digit series in the order of: growth, face, brain, and alcohol. Each characteristic is ranked on a 5-point Likert Scale. Team members of the Manitoba FASD Centre have over 20 years' experience in its use.

Clinical Tools Used in Assessments

Developmental Scales

Gesell Developmental Schedules. Preschoolers are clinically assessed by developmental pediatricians using the Revised Gesell Developmental Schedules (18). These clinical scales measure developmental status of infants and preschoolers up to 72 months. The scales provide developmental quotients (DQs) in cognitive, language, and motor domains, from which a DQ of developmental age to chronologic age can be calculated. The standardization sample is weak although newer revisions have improved the standardization.

Language

Clinical Evaluation of Language Fundamentals Preschool-2nd Edition (CELF-P2). The CELF-P2 is a standardized assessment tool used to identify and diagnose language deficits in children aged 3–6 years (19). Normative data for this test are derived from the 2000 U.S. Census population and includes preschoolers with developmental delays as well as those who have received specialized clinical services. Scoring categories include the "Core Language Score," which measures general language ability and determines a child's overall language performance, and a second category, including four "Language Index Scores," which provides more comprehensive information on language and communication, including receptive language, expressive language, language content, and language structure.

These indices are calculated using different combinations of the seven different subtest scores, which include sentence structure, word structure, expressive vocabulary, concepts and following directions, basic concepts, recalling sentences, and word classes (both receptive and expressive).

Preschool Language Scale-4th Edition (PLS-4). The PLS-4 is a standardized tool used to identify children from birth to 6 years of age who have a language deficit (20). Normative data are also derived from the 2000 U.S. Census population, including a representative sample of preschoolers with developmental delays. The PLS-4 reports two subscales: auditory comprehension (AC) and expressive communication (EC). A total test score is derived by combining the AC and EC subscales.

The severity of the language deficit for both the PLS-4 and the CELF-P2 was determined using the following scale: severe (standard score <70); moderate (standard scores between 71 and 77); mild (standard scores between 78 and 85); average (standard scores between 86 and 114); and above average (standard scores >114).

Sensory Processing

Sensory Profile (SP). The SP is a standardized tool designed to evaluate children's sensory processing skills and how it impacts their participation in meaningful and daily tasks (21). The SP assesses for sensory processing difficulties in young children, in combination with other assessments in the early diagnosis of children affected by PAE. Normative data on 1037 children include smaller samples of children with developmental disabilities. The SP is a clinically based caregiver questionnaire where the caregiver rates the frequency of the child's behavior from "never" (0% of the time), "seldom" (about 25% of the time), "occasionally" (about 50% of the time), "frequently" (about 75% of the time), to "always" (100% of the time). Results from the ratings are put into a classification system, which organizes the scores into three groups: *Typical Performance* (score at or above 1 SD below the mean), *Probable Difference* (scores at or above 2 SDs below the mean but lower than 1 SD below the mean), and *Definite Difference* (scores below 2 SDs below the mean). Scores are reported in the data per section and as an overall total score. It is possible to have a *Definite Difference* score in one area but a total score in the *Probable Difference* range.

The *Short Sensory Profile (SSP)* is a 38-item caregiver questionnaire designed for use in screening and research protocols (21). In the preschool years, the SSP can also be completed by daycare and preschool staff to provide information on sensory processing skills in different environments. A rigorous process was used to develop the SSP from the full form SP using a data sample of 117 children, both with typical development and neurodevelopmental disabilities.

Motor Assessments

Movement Assessment Battery for Children – 2 (MABC-2). The MABC-2 is a standardized tool that assists in identifying children who have motor function impairment (22). The MABC-2 reports a standard score for three components: Manual Dexterity, Aiming & Catching, and Balance, as well as a Total Test Score, with a mean standard score of 10 and standard deviation of 3. Interpretation of individual component scores and the total test score is critical and may guide intervention planning.

The Beery–Buktenica Test of Visual-Motor Integration (Beery VMI). The Beery VMI is a standardized tool that assesses visual-motor integration abilities in children (23). The Visual Perception (VP) and Motor Coordination (MC) subtests break down two important building blocks for visual motor integration (visual vs. motor functioning). For standardized administration, the Beery VMI is first followed by the VP, and finally the MC. It uses a mean standard score of 100 and a standard deviation of 15.

Executive Functioning

The Behavior Rating Inventory of Executive Function – Preschool Version (BRIEF-P).

The BRIEF-P is used to measure executive functioning (24). The BRIEF-P converts caregiver ratings into one global composite score, and three broad indexes: (a) Inhibitory Self-Control; (b) Flexibility; and (c) Emergent Metacognition. Scores are presented as *T* scores, where *T* scores ≥70 are indicative of severe impairment.

Adaptive Assessment

The Adaptive Behavior Assessment System, Third Edition (ABAS-3). The ABAS-3 is a caregiver-rated measure used to assess adaptive behaviors that are age-appropriate behaviors necessary for meeting the demands of everyday living (25). The ratings from the ABAS-3 create an overall general adaptive skills score (General Adaptive composite; GAC), and scores for each adaptive domain: (a) conceptual skills; (b) social skills; and (c) practical skills. Standard scores <70 are indicative of severe impairment.

Statistical Analysis

Descriptive statistical and multivariate analyses for prediction modeling were conducted with the support of the Centre for Healthcare Innovation (CHI) at the University of Manitoba. Independent sample *t*-tests were used to calculate differences in assessment results between preschoolers with and without FASD. For prediction analysis, missing data were predicted using regression models, with the variable in question being regressed upon every other variable in the data in an iterative process to create informed estimates of the predicted value. Following this, the separate imputed datasets were analyzed, and the results were pooled into one inference. Lastly, CHI created multivariate analyses of the data by creating a pooled logistic regression model, with FASD as the dependent variable, and multiple predictors. Results at $P < 0.05$ were considered statistically significant.

Ethics approval was received from the University of Manitoba Health Research Ethics Board #HS19754 (H2016:195).

RESULTS

Demographics and Diagnosis

There was a 1.4 male:1 female ratio in the data. An FASD diagnosis was made in 48% of males and 49% of females. The prenatal use of other substances was common in 91% of the total preschool group with PAE. Most preschoolers resided with foster families of nonkinship care at the time of the assessment (77%). An equal number of preschoolers resided with biological families (11%) and foster families of kinship care (11%), and about 1% of preschoolers lived with adoptive families.

Approximately, half of the preschoolers with PAE (51%) met clinical criteria for a diagnosis of FASD, 6% of children were diagnosed with FASD with SFF, and 43% of children were diagnosed with FASD without SFF (Figure 1).

Table 1 shows that most preschoolers did not meet the growth criteria using the 4-digit code, unless they were diagnosed with FASD (4.1%). 15.7% of preschoolers with PAE met either level 3 or 4 facial criteria, and of this group, the majority (87% of those with face coded 3 or 4) met criteria for FASD. 52.1% of preschoolers with PAE met either level 3 or 4 brain criteria, and of this group, the majority (86.4% with face coded 3 or 4) met criteria for FASD. PAE was confirmed in all children with an equal distribution between those who met the criteria for a diagnosis and those who did not.

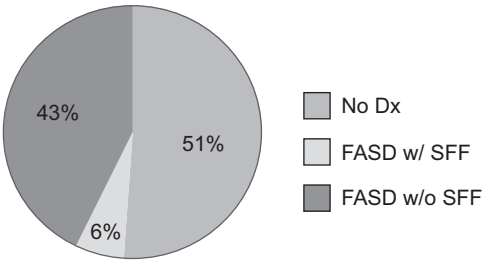

FIG 1. FASD Diagnosis for Total Sample (n = 340). SFF = sentinel facial features; w/ = with; w/o = without; FASD = Fetal Alcohol Spectrum Disorder.

TABLE 1. FASD diagnosis by 4-Digit Code: PAE No FASD Versus FASD (% Total).

Code	Growth		Face		Brain		Alcohol	
	PAE no FASD (% Total)	FASD (% Total)	PAE no FASD* (% Total)	FASD (% Total)	PAE no FASD (% Total)	FASD (% Total)	PAE no FASD (% Total)	FASD (% Total)
1	158 (46.4)	134 (39.4)	133 (39.2)	88 (25.9)	17 (5.0)	3 (0.9)	1 (0.3)	0 (0.0)
2	4 (1.2)	12 (3.5)	27 (8.0)	38 (11.2)	127 (37.4)	16 (4.7)	7 (2.1)	3 (0.9)
3	3 (0.9)	12 (3.5)	5 (1.5)	21 (6.2)	21 (6.2)	121 (35.6)	83 (24.4)	75 (22.1)
4	3 (0.9)	14 (4.1)	2 (0.6)	25 (7.4)	3 (0.9)	32 (9.4)	77 (22.6)	94 (27.6)
Subtotals	168 (49.4)	172 (50.6)	167 (49.3)	172 (50.7)	168 (49.4)	172 (50.6)	168 (49.4)	172 (50.7)
Totals	340		339		340		340	

**N=339, as the face code could not be calculated for one patient with PAE due to craniofacial difference.*
PAE = prenatal alcohol exposure; FASD = Fetal alcohol Spectrum Disorder.

Physical Features

Figure 2 shows that microcephaly was found in 10.6% of the clinical preschool population with PAE. Of these preschoolers with microcephaly, over half (57.6%) also had all three SFF. Of the group with both microcephaly and all three SFF, 94.7% also met the criteria for an FASD diagnosis.

Neurodevelopmental Assessments

Developmental Scales

Figure 3 shows that preschoolers with PAE and FASD have below average DQs. There was a significant difference in cognitive DQ for preschoolers with (M = 82.89, SD = 13.57) and without (M = 91.20, SD = 10.02) FASD; $t(267.15) = 6.06$, $P < 0.001$. Similarly, the mean language DQ was significantly lower in preschoolers with (M = 79.90, SD = 16.10) than without (M =89.83, SD = 13.15) FASD; $t(144.42) = 4.55$, $P < 0.001$. Motor scores also showed lower DQs in the preschoolers with FASD (M = 85.74, SD = 13.07), compared with those with PAE alone (M = 95.12, SD = 8.22); $t(83.12) = 4.94$, $P < 0.001$. Finally, the mean Global DQ (reflecting the combination of cognitive, language, and

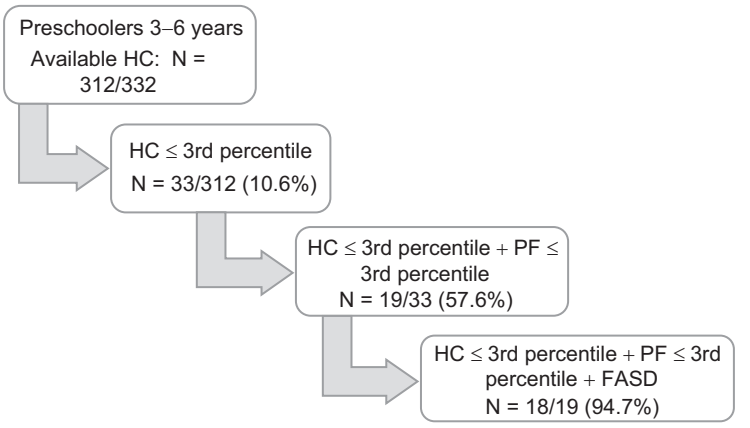

FIG 2. FASD Diagnosis by the Presence of SFF and Microcephaly (Head Circumference – HC < 3rd Percentile). PF = palpebral fissures; FASD = Fetal Alcohol Spectrum Disorder; HC = head circumference.

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motor DQs) was significantly lower in preschoolers with (M = 82.78, SD = 13.54) than without (M = 91.04, SD = 10.15) FASD; $t(267.35) = 6.01$, $P < 0.001$.

Language Scales

The mean Auditory Scores for preschoolers with FASD (M = 73.41, SD = 13.34) were lower than those without (M = 83.89, SD = 13.65), $t(77.00) = 3.45$, $P < 0.001$ (Figure 4). Preschoolers with FASD (M = 74.42, SD = 11.81) also obtained significantly lower Expressive Scores than preschoolers without FASD (M = 82.58, SD = 13.53), $t(72.00) = 2.77$, $P = 0.007$. The mean Total Language Score was also lower for preschoolers with (M = 71.47, SD = 12.58) than without (M = 81.06, SD = 14.32) FASD, $t(71.00) = 3.04$, $P < 0.001$.

To look more closely at language function, Figure 5 displays the distribution of CELF-P2 scale scores by FASD diagnostic status. Overall, the mean Core Language Index Score for those with FASD (M = 77.69, SD =14.95) was significantly lower than those without FASD (M = 86.51, SD = 14.18); $t(160.00) = 3.79$, $P < 0.001$. Similarly, there were significant differences in the Receptive Language Index Score for preschoolers with (M = 78.60, SD = 14.34) and without (M = 86.91, SD = 13.90) FASD; $t(142.00) = 3.41$, $P < 0.001$. The Expressive Language Index Score also was significantly different between those with (M = 76.82, SD = 14.75) and without (M = 84.78, SD = 14.04) FASD; $t(149.00) = 3.31$, $P = 0.001$. Preschoolers diagnosed with FASD also showed lower scores on language content ($t_{142.00} = 3.17$, $P = 0.002$) and structure ($t_{148.00} = 3.67$, $P < 0.001$) than those not diagnosed with FASD.

Motor Assessment

The total MABC-2 scores obtained by preschoolers with FASD (M = 6.58, SD = 2.84) were significantly lower than those without FASD (M = 8.44, SD = 2.95), $t(151.00) = 3.86$, $P < 0.001$ (Figure 6). There were also significant group differences for the

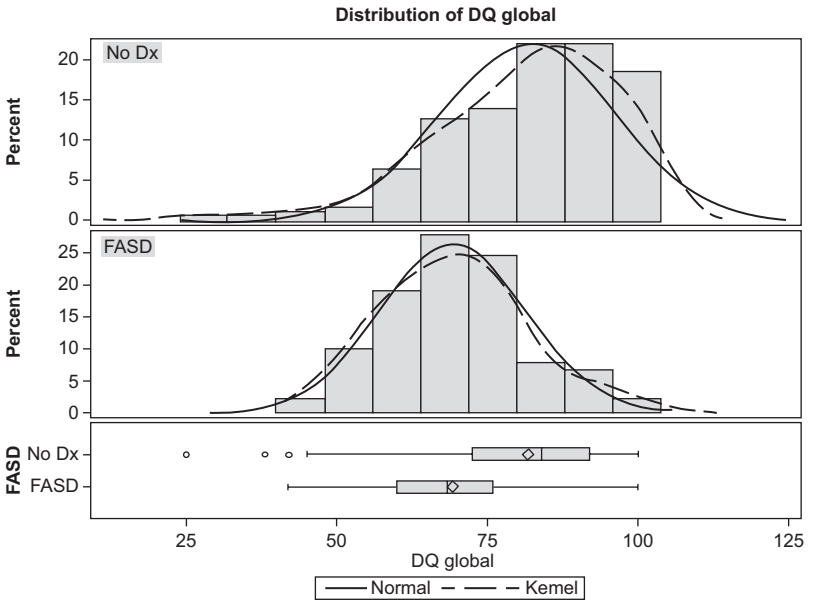

FIG 3. Global DQ by FASD Diagnostic Status. DQ = developmental quotient; FASD = Fetal Alcohol Spectrum Disorder. The black line represents the mean score of the measure. The error bars represent the SD.

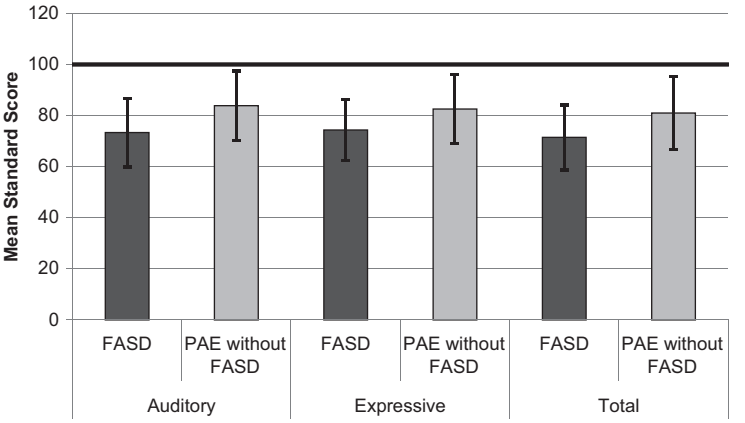

FIG 4. Distribution of PLS-4 Scale Scores by FASD Diagnostic Status. The black line represents the mean score of the measure. The error bars represent the standard deviation. PLS-4 = Preschool Language Scale-4th Edition; FASD = Fetal Alcohol Spectrum Disorder.

Manual Dexterity score ($t_{159.00}$ = 3.52, P < 0.001) and the Balance score ($t_{155.00}$ = 2.80, P = 0.006), with preschoolers with FASD obtaining lower scores (*M* = 5.77, *SD* = 2.65; *M* = 7.49, *SD* = 2.72, respectively) than their counterparts (*M* = 7.49, *SD* = 3.28; *M* = 8.90, *SD* = 3.26, respectively). The Aiming and Catching score was similar for preschoolers with (*M* = 9.57, *SD* = 3.25) and without (*M* = 10.44, *SD* = 2.91) FASD, *t*(157.00) = 1.75, P = 0.082.

Figure 7 shows that mean VMI score for preschoolers with FASD (*M* = 91.96, *SD* = 12.24) was significantly lower compared with those with PAE alone (*M* = 97.51, *SD* = 11.63), *t*(172.00) = 3.06, P = 0.003. The mean VP subtest score was also

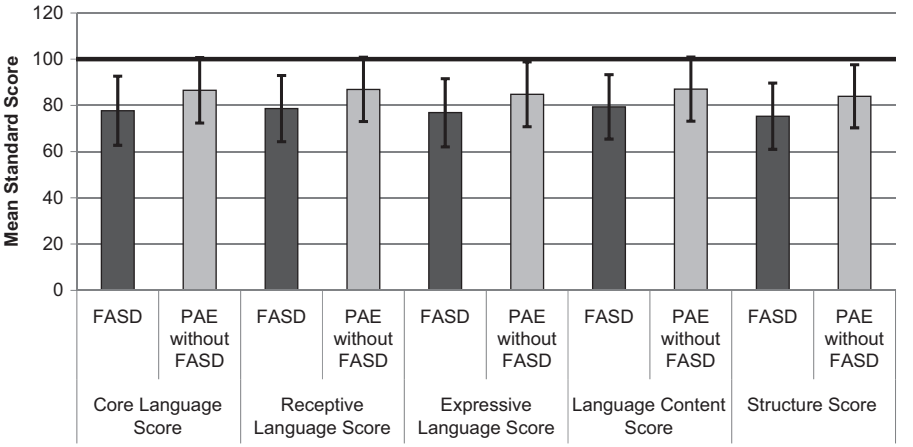

FIG 5. Distribution of Core Language and Index Scores for the CELF-P2 Scales by FASD Diagnostic Status. The black line represents the mean score of the measure. The error bars represent the standard deviation. CELF-P2 = Clinical Evaluation of Language Fundamentals Preschool-2nd Edition; FASD = Fetal Alcohol Spectrum Disorder.

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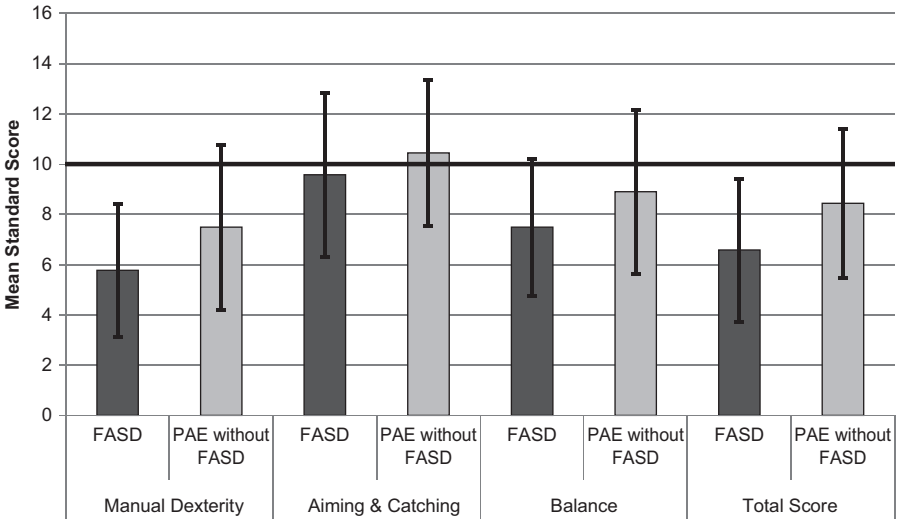

FIG 6. Distribution of MABC-2 Scores by FASD Diagnostic Status. MABC-2 = Movement Assessment Battery for Children-2nd Edition; FASD = Fetal Alcohol Spectrum Disorder. The black line represents the mean score of the measure. The error bars represent the standard deviation.

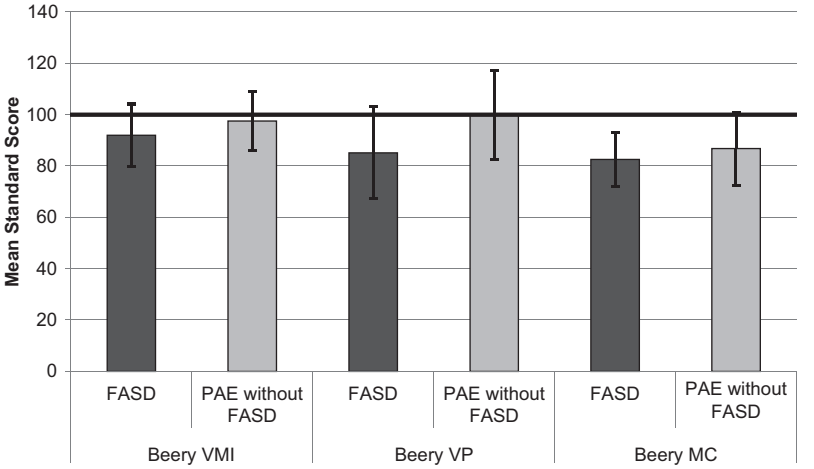

FIG 7. Distribution of Beery VMI Scales by FASD Diagnostic Status. MC = motor coordination; VMI = visual-motor integration; VP = visual perception; Beery VMI = Beery–Buktenica Test of Visual Motor-Integration; FASD = Fetal Alcohol Spectrum Disorder. The black line represents the mean score of the measure. The error bars represent the standard deviation.

significantly lower for those with FASD (M = 85.10, SD = 17.92), compared to those without FASD (M = 99.92, SD = 17.26), $t(68.00) = 3.51$, $P < 0.001$. Group difference across mean MC subtest score between those with (M = 82.58, SD = 10.63) and without (M = 86.76, SD = 14.24) FASD were nonsignificant, $t(66.00) = 1.35$, $P = 0.182$.

Sensory Processing

Figure 8 displays the risk of receiving an FASD diagnosis by SSP total score. Small cell numbers precluded in-depth analysis of sensory patterns and responses. However, there was a large difference in the number of children observed to demonstrate typical sensory response patterns with only 24% of

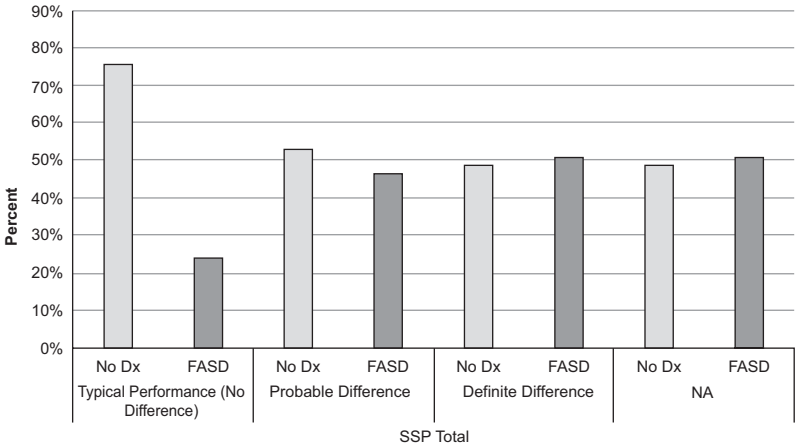

FIG 8. Risk of FASD Diagnosis by SSP Total Score. NA = score not available; SSP = Short Sensory Profile; FASD = Fetal Alcohol Spectrum Disorder.

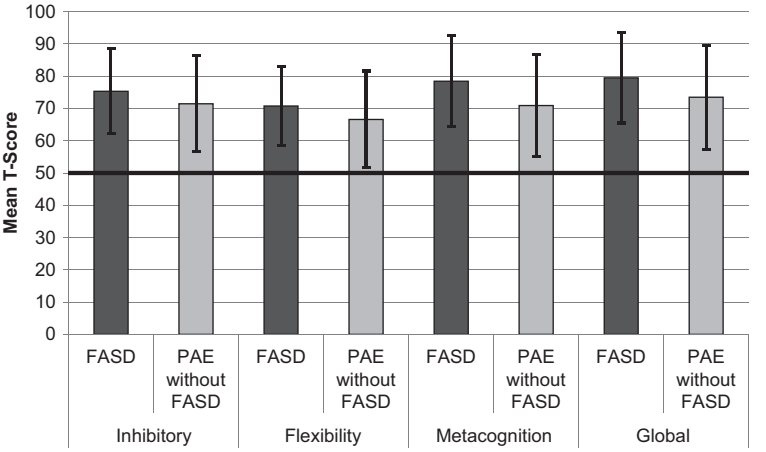

FIG 9. Distribution of Mean T-scores Across BRIEF-P Scales by FASD Diagnostic Status. The black line represents the mean score of the measure. The error bars represent the standard deviation. BRIEF-P = Behavior Rating Inventory of Executive Functioning – Preschool; FASD = Fetal Alcohol Spectrum Disorder.

preschoolers with FASD showing typical response patterns, compared to 76% of preschoolers with PAE. Within the category of "definite differences," there was a more even split with 51% of preschoolers with FASD versus 49% of those with PAE alone, clearly showing different response patterns.

Behavior: Executive Functioning

Figure 9 shows that all preschoolers with PAE had challenges applying executive functioning skills, irrespective of an FASD diagnosis. There were significant differences in the mean Global Index score between preschoolers with (M = 79.46, SD = 13.94) and without (M = 73.47, SD = 16.17) FASD, $t(158.80) = -2.58$, P = 0.011. Preschoolers with FASD had significantly higher scores on the Metacognition Index (M = 78.45, SD = 14.16), compared to their counterparts (M = 70.88, SD = 15.89), $t(169.00) = -3.30$, P = 0.001. The Inhibitory Index ($t_{169.00} = -1.80$, P = 0.074) and the Flexibility Index

($t_{155.16}$ = –1.97, P = 0.051) scores were comparable across groups.

Adaptive Functioning

Figure 10 shows that the GAC reported for preschool children with FASD (*M* = 67.32, *SD* = 12.74) was significantly lower than those without FASD (*M* = 75.34, *SD* =13.75), *t*(94.00) = 2.80, P = 0.006. Similar patterns were noted for preschoolers with FASD across the Conceptual ($t_{96.00}$ = 2.89, P = 0.005) and Practical ($t_{96.00}$ = 2.57, P = 0.012) skill domains, with preschoolers with FASD (*M* = 69.03, *SD* = 13.39; *M* = 66.46, *SD* = 14.02, respectively) obtaining lower scores than preschoolers with PAE alone (*M* = 77.46, *SD* = 14.35; *M* = 73.84, *SD* = 13.65, respectively). Reported social skills were found to be comparable between preschoolers with (*M* = 75.48, *SD* = 15.80) and without (*M* = 79.00, *SD* = 13.97) FASD, *t*(99.00) = 1.18, P = 0.242.

Predictive multivariate regression analysis. Table 2 shows the results of pooled multivariate analysis modeling of domain variables predictive of FASD diagnosis in preschoolers. Motor functioning (Total MABC-2 score), language skills (Core Language Score; CELF-P2), and the presence of sensory processing differences (SSP Total) were found to be significant predictors of FASD diagnosis. Significant strength reflected in the sensory variable was also found, supporting global sensory processing differences as a particularly important predictor of FASD diagnosis in preschoolers.

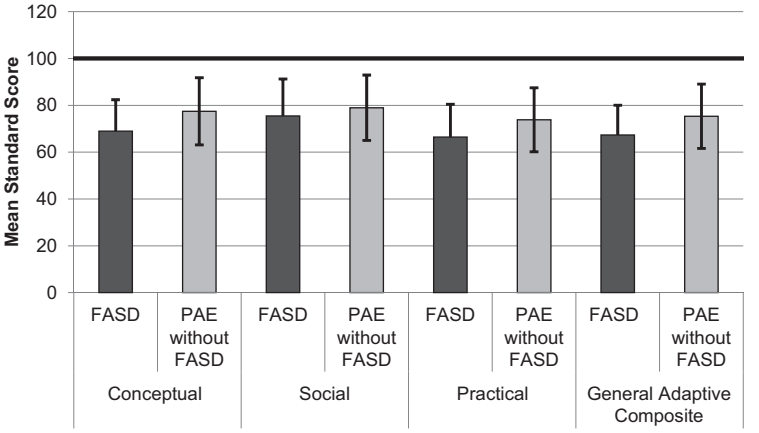

FIG 10. Distribution of Scores on the ABAS-3 Scales by FASD Diagnostic Status. The black line represents the mean score of the measure. The error bars represent the standard deviation. ABAS-3 = Adaptive Behavior Assessment System, Third Edition; FASD = Fetal Alcohol Spectrum Disorder; PAE = prenatal alcohol exposure.

Table 2. Pooled multivariate analyses: significant factors upon mutual adjustment.

	Odds ratio (95% CI)	***df***	**P**	**nmis**
Total MABC2 score	0.88 (0.76, 1.0)	26.79	0.067	80
Core Language score	0.95 (0.93, 0.98)	62.90	<0.001	63
Sensory 2	3.13 (1.62, 6.05)	194.63	<0.001	NA

df = degrees of freedom; nmis = number of missing observations.
Source: Adapted from FASD prediction models from CHI.

DISCUSSION

This study presents data underscoring the importance of early diagnostic multidisciplinary assessment of preschoolers with PAE. It shows that in combination, clinically significant deficits in communication, motor skills, and sensory processing are predictive of a diagnosis of FASD and can, therefore, be clinically used to support early diagnosis in the preschool period. Clinicians can then improve management by offering areas for targeted intervention to improve outcomes from an early age and reduce the burden of care on families.

In Manitoba, preschoolers make up 19% of the children seen for the assessment of FASD. Of these preschoolers, 23% received a diagnosis of FASD with SFF, 22% received a diagnosis of FASD without facial features, and 55% did not receive an FASD diagnosis. Commonest concerns prompting referral of preschoolers with PAE in Manitoba included dysregulation (77%) and developmental delays (57%). Brain domain impairments that were found to be the most prevalent in preschoolers diagnosed with FASD were executive functioning (76%), attention (72%), motor (62%), adaptive (55%), and language (52%). Impairments in the motor domain distinguished those preschoolers who met the criteria for a diagnosis of FASD from those who did not. Among preschoolers who were not diagnosed, only 21% demonstrated impairment in attention, and 13% had executive functioning impairments. Only children who met the criteria for a diagnosis showed significant impairments in the adaptive domain. Children with an at-risk designation tended to have slightly higher rates of impairments in adaptive functioning (17%) and executive functioning (17%), and slightly lower impairment in attention (17%).

The following discussion reflects the results of our study organized by brain domains:

1. **Cognition development and neurophysiology/neuroanatomy –**
   Cognitive problems have been consistently found in preschoolers with FASD (2). In Manitoba, 22% of preschoolers assessed demonstrated significant cognitive developmental impairments. These findings are consistent with other studies, such as McLachlan et al. (4), which found cognitive impairments in over a third of the preschoolers with PAE.

   Measurement of occipitofrontal diameter plotted on standardized head circumference curves is a good proxy measure of brain growth and volume. Microcephaly was originally described as a feature of Fetal Alcohol Syndrome (FAS) by Jones and Smith (26), and Lemoine et al. (27). Microcephaly was seen in approximately 10% of our sample of preschoolers with PAE. Of this group, 83% met criteria for FASD, making microcephaly a clinically significant early finding. This also means that most preschoolers have normal head circumferences and show impairments in other neurobehavioral domains, necessitating a comprehensive multidisciplinary assessment.

2. **Language –**
   Our study shows significant receptive and expressive language impairment in preschoolers with PAE, with more significant impairments evident in children who met the diagnostic criteria for FASD. We also found that impaired language in combination with developmental impairments in motor skills and sensory processing is a significant predictor of FASD and supports a neurotoxic effect of alcohol on the developing brain. Research has shown that children with FASD have numerous delays and impairments in aspects of language development, including speed acquisition, speech production, and receptive and expressive language (2). Research examining the communication skills of preschool children found that language deficits at

4 years of age can be reliably identified prior to the child's second birthday in approximately 80% of the children (28). Another study examining children between the ages of 4 and 58 months found that all participants with FASD showed language impairment, communication delay, verbosity, and some processing disorder (29). These results were consistent with another study on preschool children, which also found that children with FASD had significantly impaired communication skills (4).

3. **Motor skills and sensory development –** Our study data show that motor development and sensory processing together with language predict FASD diagnosis in the absence of classical dysmorphology and are important to include in the comprehensive assessment of preschoolers. These results are consistent with previous research, which has shown significant deficits in motor skills and sensory development in children with FASD (2). Fine motor skills have been shown to be significantly impaired, compared to gross motor skills, particularly with moderate to high level PAE, compared with low PAE (30–32). Fine motor steadiness and increased alcohol exposure have been shown to have a positive association, suggesting a dose–response relationship (2). Compared with other fine motor skills, complex fine motor skills, such as visual-motor development, showed significant deficits, compared to other motor skills (2). Consistent with our results, Doney et al. (32) highlighted the importance of administering the full Beery VMI assessment, including both VP and MC subtests, for diagnostic purposes as well as intervention planning.

Our clinical data show a correlation between sensory processing differences with FASD diagnosis; 83% of preschoolers seen for an FASD assessment in Manitoba were found to have significant differences in sensory sensitivities and processing, while only 58% of at-risk preschoolers and 38% of preschoolers with no FASD diagnosis showed significant differences. Sensory processing differences in visual, auditory, tactile, auditory filtering, underresponsiveness to sensory information, and sensation-seeking behaviors have been shown to be clinically significant in children with FASD (33–36). The neurologic correlates of sensory processing behaviors relate to white matter development, which is sensitive to PAE (37–40). In a therapeutic environment, understanding sensory processing patterns can contribute to a better understanding of unregulated behavior and foster the development of self-regulation and adaptive behaviors in toddlers (41). Currently, the Canadian guidelines do not include sensory processing as a brain domain for the assessment of FASD. Our results support the inclusion of sensory processing in the preschool battery of assessments in the Canadian guidelines for FASD diagnosis as an independent and sensitive measure, reflecting neurological integrity in young children informing a comprehensive and developmentally appropriate assessment profile.

4. **Executive functioning and attention –** Executive functioning impacts many brain domains and is assessable in younger children (42, 43). Our findings show global deficits in executive functioning that are measurable in preschool children with PAE/FASD. The results of our study are consistent with previous research indicating that young children with FASD demonstrate executive functioning deficits including disruptions in inhibition and cognitive flexibility (44). Fuglestad et al. (44) also

found an association between the severity of executive functioning deficits and the severity of FASD. A Canadian study of preschoolers also showed that most preschool children demonstrated significantly impaired executive functioning (4). Understanding the severity of executive functioning deficits among preschoolers with FASD is important for early intervention given that these difficulties have been found to impact social competence later in life (44). All of these findings are consistent with research on executive functioning in older children with FASD and support the importance of early assessment to inform appropriate intervention.

5. **Adaptive functioning, social skills, and social communication –**

We found that compared to preschool children without FASD, preschool children with FASD had significantly lower caregiver-ratings of overall adaptive skills, conceptual skills, and practical skills. These findings are largely consistent with previous research on younger and older children (45). A number of studies suggest that adaptive functioning, social skills, and social communication deficits are evident not only in older children with PAE but also in up to half of younger children as well (2, 4). Our study found that preschoolers diagnosed with FASD showed lower social skills than those with PAE who did not receive a diagnosis, although group differences did not reach statistical significance. This may reflect a common disorganizing impact of PAE on preschool behavior, which is more specifically measurable at older more independent ages when the threshold for FASD diagnosis has been met and the demands of the environment for independent functioning become more evident (46, 47). Other research has shown that adaptive behavior and social skills among preschoolers with FASD were lower than expected for their age, and deficits in global functioning can become more pronounced with age (2, 45). Preschool children with FASD may struggle with using appropriate language in social situations (46). These social skill struggles manifest as higher order language skills deficits later in life (2). Young children with FASD have been shown to have difficulties with emotional processing, social cognition, increased activity levels, and behavior problems (48, 49). Preschoolers with PAE showed more deficits on caregiver ratings internalizing problems and being more emotionally withdrawn than nonexposed children (50, 51). Challenges with social–emotional organization and control are important cues for early assessment of adaptive functioning in preschoolers with PAE and offer opportunities for early intervention for the children and support for their caregivers.

Other Clinical Considerations

Clinical confidence in the assessment of preschoolers is affected by clinician experience and described patterns in large cohorts of clinical samples (52). This study describes a large, 10-year cohort of children clinically assessed by a multidisciplinary team experienced in the assessment of children with PAE and in FASD diagnosis. All children seen in this clinic have undergone rigorous confirmation of PAE and have presented with neurobehavioral concerns at the time of assessment. In our cohort, approximately half of the children aged 3–6 years met the criteria for a diagnosis of FASD. In preschoolers with PAE, microcephaly and all three SFF are sensitive signs distinguishing those who meet the criteria for an FASD diagnosis.

In addition to the consideration of clinically significant domain scores in preschoolers, it is important not to dismiss scores that do not reach clinical

significance but are informative for intervention. Our study found that functional domains of global development, language, motor skills, executive functioning, and adaptive functioning were consistently lower for children with PAE than those without PAE. Furthermore, when comparing children with PAE who did not receive an FASD diagnosis to those who did receive a FASD diagnosis, those with FASD consistently showed poorer functioning. This finding suggests either a grading of effects related to the specifics of PAE (such as dose or timing) or preclinical effects in at-risk children supporting longitudinal follow-up.

Elevations in scores that do not meet clinical thresholds are still important to inform early intervention and longitudinal monitoring, as many of these factors are associated with a future diagnosis of FASD. Almost half of the children that had a probable difference and a definite difference are at risk of being diagnosed with FASD in the future. Even among predictive factors, such as sensory processing, lower scores were of significance, and about 30% of those who had a positive sensory score were at risk of receiving an FASD diagnosis in the future.

Limitations

This study is a 10-year retrospective review of clinical data and not a prospective study of developmental outcomes of PAE in preschoolers. Our results are therefore limited by the clinical data available, including missing data due to assessment and guideline changes. The clinical data do not include imaging or genetic findings, which would be important additional investigations for future study. Although our overall sample size was large, some of the nonsignificant findings may be due to low numbers in specific variables (low power). A larger sample size with more detailed data collected would allow for analysis of the impacts of multiple exposures and adverse childhood experiences on developmental outcomes. Finally, our sample only consisted of preschool children with PAE. A comparison with comprehensive assessments of children with other neurodevelopmental disabilities would inform both assessment as well as intervention strategies.

IMPLICATIONS AND FUTURE RESEARCH

Early intervention is important in reducing the impact of risk factors such as PAE on neurobehavioral outcomes of children while supporting and enhancing protective factors (2). A multidisciplinary team is recommended in the assessment of preschoolers at risk, as this assessment will inform a spectrum of individually and developmentally appropriate interventions. The assessment of preschoolers with PAE demonstrating neurobehavioral deficits should include specialized assessments of communication, motor skills, cognitive development, sensory processing, and neurobehavioral functioning, including executive and adaptive functioning. Sensory processing is a measure of neurological development and integrity, and our study further demonstrated that sensory processing is particularly important in the assessment of young children, where the relative importance of these neurological tracts clearly impacts behavior. The functional impact of these skills is reflected in subsequent measures of adaptive functioning, and this should be carefully and clinically assessed.

There is a need for multisite longitudinal studies on preschool-aged children, as well as on interventions they receive to show the differences made in the children's lives (53, 54). There is also a need for further study of appropriate assessment procedures for preschool children undergoing FASD assessment (4). Prospective studies on preschoolers exposed to complex risk factors are important to further our understanding of the impacts of these factors and, most importantly, to inform societal understanding and appropriate supports to families who care for them.

The assessment of preschoolers at risk based on a history of exposures to substances, trauma, and toxic stressors is critical to inform early intervention,

potentially decrease the severity of deficits later in life, and improve outcomes. Preschool children with confirmed PAE who demonstrate difficulties in motor, language, and behaviors, which may be attributable to differences in sensory responsivity, should be considered for comprehensive FASD diagnostic assessment. Early recognition and diagnostic assessment are critical for providing appropriate management and dedicated support to these children and their families.

CONCLUSIONS

This study describes the multidisciplinary assessment of the largest cohort of preschool children with PAE published till date. Clinical data show that preschoolers with FASD demonstrate global impairments in functioning, which is greater than in those with PAE alone. Data also provide new evidence for including sensory processing in the diagnostic guidelines as a sensitive measure of FASD in the preschool population. Importantly, this study also shows that the combination of significant impairments in motor, language, and sensory processing is able to predict FASD diagnosis in preschoolers. The evidence in this study supports early comprehensive assessment of cognitive and behavioral functioning in preschoolers with PAE to inform appropriate diagnosis, intervention, and to support optimal outcomes.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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DATA AVAILABILITY STATEMENT

The clinical data are the property of the Manitoba FASD Centre/Rehabilitation Centre for Children.

COMPLIANCE WITH ETHICAL STANDARDS

This study was approved by the University of Manitoba Health Research Ethics Board (HREB).

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