Risk Factor of Birth Weight below 2,500 Grams and Attention Deficit Hyperactivity Disorder in Thai Children

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Objectives: *To study the factor of birth weight below 2,500 grams and Attention Deficit Hyperactivity Disorder (ADHD) and to identify the factors that are associated with ADHD.*
Material and Method: *A retrospective, hospital – based, case control study was conducted with 122 ADHD cases from the child and adolescent psychiatric outpatient unit at Siriraj Hospital, 119 nonADHD from students who have been assessed from Child Behavior Checklist (CBCL) and Conners Teacher Rating Scale, they are identified as normal. Mothers of both groups have been asked to fill a self report questionnaire to evaluate demographic data, prenatal data, factors effected pregnancy both physical and mental illness, post natal period, birth weight, underlying disease, physical illness and family history of ADHD. Multiple logistic regression analysis was used to determine the adjust effect of all factors.*
Results: *The number of ADHD cases who had a birth weight below 2,500 grams was 3.6 times the number of control cases who had a birth weight below 2,500 grams. It was statistically significant (p = 0.03). Factors associated with ADHD were pregnancy complication (p value < 0.05, OR = 4.17, 95%CI [1.66, 14.02]), emotional distress during pregnancy (p value <0.05, OR = 2.99, 95%CI [1.43, 5.40]), postnatal complication (p value < 0.05, OR = 3.26, 95%CI [1.56, 6.41] and a family history of ADHD (p value < 0.05, OR = 3.6, 95%CI [1.65, 8.11].*
Conclusion: *From the present study, the birth weight below 2,500 grams, pregnancy complication, emotional distress during pregnancy, neonatal complication and a family history of ADHD may be the risk factors of ADHD.*

Keywords: *ADHD, Birth weight, Perinatal complication, Pregnancy complication*

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Attention deficit hyperactivity disorder (ADHD) is one of the most common behavioral problems in child and adolescent psychiatric disorders[1,2]. In Thailand, the prevalence is about 5 percent[3]. Although etiology and risk factors of ADHD are unclear, there is a lot of clinical evidences showing the causes and risk factors of ADHD[4-7]. A previous study showed that birth weight is one of the important factors of ADHD[8-14]. Low birth weight infants are commonly found to have both cognitive and behavioral problems in childhood[8-11], Telpin found a 3 fold increased risk for ADHD associated with extremely low birth weight (BW < 1,000 gm)[12]. Breslau found a very low birth weight (BW < 1,500 gm) which has both internalizing and externalizing behavior more than children with a normal birth weight[13]. The latest study by Mick found ADHD with a birth weight below 2,500 grams was 3 times more common than ADHD of the general population[14].

The objectives of the present study, a clinical hospital-based approach, were to identify the risk

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factor of birth weight below 2,500 grams and ADHD and to analyze factors associated with ADHD.

Material and Method

The presented case control, a retrospective study, was conducted at the outpatient department of the child and adolescent psychiatric unit, Siriraj Hospital. The protocol was approved by the Ethical Committee on Research Involving Human Subjects of the Faculty of Medicine, Siriraj Hospital, Mahidol University. The study subjects comprised of 122 ADHD patients, both of old and new cases and 119 control cases.

Inclusion criteria of the study group were the followings:

1. Age 6-12 years old.
2. The clinical diagnosis of ADHD was strictly based on DSM-IV TR criteria by both the authors, the intraobservation and another psychiatrist, the extraobservation.
3. T score of Conners Teacher Rating Scale was above 65 in hyperactivity domain and hyperactivity index.
4. The parents of the ADHD children understand the Thai language well.
5. Parental consent form was obtained.

Exclusion criteria of study group were the followings:

1. Children who had other diagnoses in Axis I in DSM IV TR criteria.
2. Mental retardation.
3. Parental problem with perception or interpretation such as psychotic disorder.
4. Parental problem with communication, such as deafness.

The study cases comprised of 119 children from Kositsamosorn Primary School, the school of the mental health project.

Inclusion criteria of control group were the followings:

1. Age 6-12 years old.
2. No behavioral problems, score from CBCL screening test which have been filled by their parents. The score had to be ≤ 48 in boys and ≤ 47 in girls.
3. No suspected behavior of ADHD, T score from Conners teacher rating scale was below 50.
4. The parents of the children understand the Thai language well.
5. Parental consent form was obtained.

Exclusion criteria of the control group were the followings:

1. Children who had other diagnoses in Axis I in DSM-IV TR criteria.
2. Mental Retardation.
3. Parental problem with perception or interpretation, such as psychotic disorder.
4. Parental problem with communication, such as deafness.

The authors discussed in detail the study protocol with the parents of all the children before obtaining the written consent form. The data-collecting tool was a study questionnaire that has been constructed for the parents to fill. The questionnaire consisted of two parts; the first part was about the subject's mother: mother's demographic data, aged when mother got pregnant, medical complication, pregnancy complication, medication, smoking and alcohol consumption during their pregnancy, physical injury, emotional distress and labour complication. The second part was about the child including the birth weight, complication during neonatal period, underlying disease, history of seizure, head trauma, encephalitis, medication and family history of ADHD. All items were yes, no and another choice of answer. If the mother selected yes, the details of the answer should be filled.

Statistical Analyses

Statistical analyses were performed by SPSS version 11. Categorical data was shown as percent and compared between the 2 groups by Chi-square test. Continuous data were shown as mean $\pm$ SD and compared between the 2 groups by Student's t-test. The odds ratio and 95% confidence interval (95%CI) were used to compare the association between the factors and ADHD, and multiple logistic regression was used to evaluate the strength of association between factors and ADHD. A p value of less than 0.05 was considered to have statistically significant difference.

Results

There were 122 ADHD cases and 119 control cases. There was no difference in the gender and age

Table 1. Sex of the study samples

Sex	Control (N = 119)	Case (N = 122)
Boy	106 (89.1%)	106 (86.9%)
Girl	13 (10.9%)	16 (13.1%)
Total	119 (100%)	122 (100%)

Table 2. Factors associated with ADHD

	Odds Ratio	95%CI	p-value
Birth weight			0.03*
Neonatal complication	4.32	[2.19, 8.63]	<0.05
Underlying disease	0.80	[0.30, 2.00]	0.596
Convulsion, seizure	1.70	[0.90, 2.70]	0.07
CNS infection	0.90	[0.95, 3.20]	0.494
Significant head trauma	1.00	-	1.00
Current medication	1.18	[0.30, 3.54]	0.871
Family history of ADHD	4.27	[1.96, 9.50]	<0.05
Maternal age of pregnancy	1.99	[1.03, 3.88]	0.409
Pregnancy complication	5.58	[1.92, 17.40]	0.0004
Medication during pregnancy	2.72	[1.08, 7.07]	0.032
Maternal smoking	2.47	[0.12, 14.3]	0.446
Maternal alcohol drinking	1.00	-	1.00
Physical trauma	9.40	[1.19, 201.22]	0.019
Emotional distress	4.49	[2.37, 8.45]	<0.0001
Preterm, term, postterm	1.89	[0.86, 4.21]	0.122
Labour complication	0.609	[0.430, 5.401]	0.236

* one tailed analyses

distribution of the 2 groups. Mean age of the study subjects was 8.73 $\pm$ 2 years and 8.91 $\pm$ 1.9 years in control subject ($p > 0.05$).

The authors found only 3 children (2.5%) in the nonADHD groups and 11 children (9.02%) in the ADHD group who had a birth weight < 2,500 grams. In the eleven ADHD children, their birth weight were 1,600 grams, 1,800 grams 1,630 grams, 2,000 grams, 2,100 grams (2 cases), 2,200 grams (2 cases), 2,300 grams, 2400 grams and 2,450 grams respectively. In non ADHD, the three children, their birth weights were 2,350 grams (2 cases) and 2,400 grams.

Table 3. Multiple logistic regression analysis of factors associated with ADHD

	p-value	95%CI
Maternal age of pregnancy	0.066	[0.957,3.896]
Pregnancy complication	0.004	[1.661,14.022]
Medication during pregnancy	0.437	[0.184,2.081]
Physical trauma	0.067	[0.866,73.985]
Maternal emotional distress	0.003	[1.430,5.401]
Neonatal complication	0.001	[1.566,6.410]
Family history of ADHD	0.002	[1.653,8.117]

Discussion

The present study found most of the ADHD children in the child and adolescent psychiatric outpatient unit were male. The ratio between male and female children in the present study was 8:1. This result confirmed the previous knowledge that ADHD is more common in boys than girls. It may be from the clinical symptoms and signs of male ADHD are more obvious in that of hyperactivity and impulsivity than in females. Another form of ADHD that is an inattentive type is common in females which is difficult to detect by their parents and teachers and does not gain any attention by the neighboring persons. Therefore, it should be mentioned that because of the disturbing behavior to the commune makes the incidence of referring ADHD more common in males than in females in the tertiary care unit.

The present study found most of the cases in both groups had a birth weight between 2,500-3,000 grams. The number of children who had a birth weight below 2,500 grams in the ADHD group (11 cases) was almost 4 fold of the nonADHD group (3 cases) and it was statistically significantly different ($p = 0.03$). The authors also noted that the children who had a birth weight below 2,500 grams with ADHD had a mean birth weight less than the nonADHD group and according to the presented data, there was a higher prevalence of preterm labour in ADHD than nonADHD. The finding corresponded to the previous study of Mick who found low birth weight (birth weight below 2,500 grams) which was an independent risk factor associated with ADHD[14].

The other risk factors associated with ADHD were the complication of pregnancy, the maternal emotional distress which included feeling stressed, anxious, depressed during pregnancy, the complication of neonatal period and the family history of ADHD were associated with the cases of ADHD. All the above mentioned risk factors in the present study were statistically significantly different (Table 2).

The complication of pregnancy associated with ADHD in the study of Milberger was bleeding per vagina[15]. The presented study found that the number of cases of bleeding per vagina in both groups were similar. But the number of cases with hyperemisis gravidarum, hypertensive disorder in pregnancy, diabetes mellitus during pregnancy was higher in the ADHD group.

Maternal emotional distress during pregnancy was also associated with ADHD, as in the study of Benjaporn who found psychiatric disorder and substance use disorder associated with ADHD[3]. Milberger[15] found ADHD associated with a serious family problem during pregnancy such as an uneasy family life, relative barrier, religious belief and mixed blood culture, etc[15]. Even though the impact of psychosocial stress in the previous studies has been weakened by the study design, it has been shown that the level of cathecolamines was increased in stress conditions[3,15,16]. In pregnant mice, it was shown that cathecolamines caused uterine vasoconstriction, which in turn produced fetal hypoxia[16]. The present data of a positive association between neonatal complication and ADHD is consistent with the findings in the previous investigation. Sato found the Apgar score of neonates at 5 minutes was statistically significantly associated with ADHD[17]. The present study found more prevalence of hyperbilirubinemia and the history of incubator treatment in the ADHD group than the nonADHD group. These findings need further study.

Family history of ADHD was also associated with ADHD in the present study. There were many studies about the clinical and molecular genetics in ADHD. They concluded that ADHD was usually found in the same family tree. The heritability value of ADHD was about 8.0 (range 0.5-0.98)[18]. Biederman also reported a 3-5 fold increased risk of ADHD in siblings of ADHD[19].

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ปัจจัยเสี่ยงในเด็กที่มีน้ำหนักแรกเกิดน้อยกว่า 2,500 กรัมต่อการเกิดโรคซน สมาธิสั้น

ชดาพิมพ์ ศศลักษณานนท์, ฐิตวี แก้วพรสวรรค์

วัตถุประสงค์*: เพื่อศึกษาว่าภาวะเด็กน้ำหนักแรกเกิดน้อยกว่า 2,500 กรัมเป็นปัจจัยเสี่ยงกับการเกิดโรคซน สมาธิสั้นหรือไม่ ในเด็กที่ได้รับการวินิจฉัยและเข้ารับการรักษาที่แผนกผู้ป่วยนอก หน่วยจิตเวชเด็กและวัยรุ่น ร.พ.ศิริราช และเป็นการศึกษาข้อมูลเพื่อเปรียบเทียบปัจจัยต่าง ๆ ที่มีอาจมีความสัมพันธ์กับการเกิดโรคซน สมาธิสั้น*

วัสดุและวิธีการ*: เป็นการศึกษาเชิงสังเกต และเชิงวิเคราะห์ โดยกลุ่มศึกษา คือ ผู้ป่วยที่เข้ารับการรักษาที่แผนกผู้ป่วยนอกของหน่วยจิตเวชเด็ก ของ ร.พ. ศิริราช ในช่วง พ.ศ.2547 จำนวนทั้งสิ้น 122 คน และกลุ่มควบคุมคือ นักเรียนที่ผ่านการประเมินว่าไม่มีพฤติกรรมที่สงสัยโรคซน สมาธิสั้นหรือพฤติกรรมที่สงสัยโรคอื่น ๆ ทางจิตเวชจาก แบบประเมิน CBCL ที่กรอกโดยผู้ปกครอง และ Conners Teacher Rating Scale ที่กรอกโดยครู จำนวน 119 คน ในการเก็บข้อมูลจะเป็นการให้มารดาตอบแบบสอบถามที่ผู้วิจัยสร้างขึ้น เพื่อรวบรวมข้อมูลส่วนบุคคลของมารดา ข้อมูลระหว่างมารดาตั้งครรภ์ ปัจจัยที่มีผลต่อการตั้งครรภ์ ทั้งปัจจัยทางด้านร่างกายและจิตใจ ปัจจัยในตัวบุตรตั้งแต่แรกเกิดและปัจจัยที่อาจมีผลต่อการเกิดโรคซน สมาธิสั้น ใช้ multiple logistic regression ในการวิเคราะห์หาความสัมพันธ์ระหว่างน้ำหนักแรกเกิด และปัจจัยอื่น ๆ กับโรคซน สมาธิสั้น*

ผลการศึกษา*: พบจำนวนของเด็กที่มีน้ำหนักแรกเกิดที่น้อยกว่า 2,500 กรัมในกลุ่มเด็กที่เป็นโรคซน สมาธิสั้นมากกว่าในกลุ่มประชากรควบคุมอย่างมีนัยสำคัญทางสถิติ (p value = 0.03) และพบปัจจัยที่มีความสัมพันธ์ กับโรคสมาธิสั้น ได้แก่ ภาวะแทรกซ้อนระหว่างตั้งครรภ์ (p value < 0.05, OR = 4.17, 95%CI [1.66, 14.02]) ภาวะอารมณ์ผิดปกติของมารดาระหว่างตั้งครรภ์ (p value < 0.05, OR = 2.99, 95%CI [1.43, 5.40]) ภาวะแทรกซ้อนในระยะแรกเกิดของบุตร (p value < 0.05, OR = 3.26, 95%CI [1.56, 6.41] และประวัติครอบครัวของโรคสมาธิสั้น (p value < 0.05, OR = 3.6, 95%CI [1.65, 8.11]*

สรุป*: น้ำหนักแรกเกิดที่น้อยกว่า 2,500 กรัมอาจเป็นปัจจัยเสี่ยงต่อโรคซน สมาธิสั้น และพบปัจจัยอื่น ๆ ที่มีความสัมพันธ์กับโรคซน สมาธิสั้น ซึ่งสอดคล้องกับการศึกษาในต่างประเทศ*