



Title	A preliminary investigation of prenatal stress and risk of autism spectrum disorder
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A Preliminary Investigation of Prenatal Stress and Risk of Autism Spectrum Disorder

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Abstract

This paper was a retrospective survey investigating the association between prenatal stress and risk of ASD in Chinese population. Twenty-eight mothers of children diagnosed with ASD, and thirty-eight mothers of children with no diagnoses of neurodevelopmental diseases were interviewed. The survey mainly investigated the incidence and intensity of prenatal stress, birth conditions and developmental problems of children, maternal health conditions, and the participants' coping strategies towards prenatal stress. Higher overall intensity and higher incidence of prenatal stress were found to be experienced by mothers of ASD children. The ASD group also showed higher incidence of prematurity, birth complications, health problems, maternal illnesses, advanced maternal age, and developmental problems. This proposed prenatal stress as a possible risk factor of ASD and the other developmental problems associated with ASD.

A preliminary investigation of prenatal stress and risk of Autism Spectrum Disorder

Autism Spectrum Disorder (ASD) is a spectrum of neuropsychological conditions characterized by widespread abnormalities in reciprocal social interaction, verbal and nonverbal communication, and restricted, repetitive and stereotyped behavior (World Health Organization, 2006). It has led to significant life-long impairments in social and language functioning for the affected individuals and significant distress for their caregivers. The prevalence of ASD was 52 per 10000 in United States (Gurney, Fritz, Ness, Sievers, Newschaffer & Shapiro, 2003), 58.7 per 10000 in United Kingdom (Chakrabarti & Fombonne, 2005), and 39.2 per 10000 in Australia (Icasiano, Hewson, Machet, Cooper and Marshall, 2004). No nationwide epidemiological study about the prevalence of ASD have been conducted in China but the prevalence of ASD in Hong Kong have been studied in a ten years study by Wong & Hui (2008) in the time period from 1985 to 2005 and was found to be 16.1 per 10000. All these findings also suggested the changing epidemiology of ASD with increasing prevalence rate compared with data from the last century (Chakrabarti & Fombonne, 2005; Gurney *et al.*, 2003; Icasiano *et al.*, 2004; Wong & Hui, 2008). Though ASD was a devastating disorder with high prevalence in different countries all over the world, its etiology was only understood in small percentage of cases and little was known about the incidence and development of ASD.

The causality of ASD has been a controversial topic since 1970s. The concordance rates in monozygotic twin pairs were found to be much higher than those for dizygotic twin pairs (Foistein & Rutter, 1997; Ritvo, Freeman, Mason-Brothers, Mo, & Ritvo, 1985). Foistein and Piven (1991) also found out higher incidence of ASD in siblings and family members of affected children He also suggested ASD was often associated with a few particular genetic disorders. All these proposed an important role of genetic factor in etiology of ASD which was also supported

by several genetic association studies (Freitag, 2007; Maestrini, Paul, Monaco, & Bailey, 2000; Muhle, Trentacoste, Rapin, 2004; Trottier, Srivastava, & Walker, 1999).

However, the concordance rates in monozygotic twin pairs in all these studies were less than 100% (Foistein & Rutter, 1997; Ritvo *et al.*, 1985). This reflected that genetic factor was not the only factor contributing to the development of ASD. In addition to the genetic part, the high similarity of prenatal and postnatal environment may contribute to the high concordance rate of ASD in monozygotic twins. The higher risk of ASD in siblings of affected children may also be the result of exposure to similar environment. Moreover, Smalley, Asarnow, & Spence (1988) suggested ASD was a non-Mendelian disorder in which the expressivity of carriers of susceptibility genes was affected by environmental risk factors. These findings raised the possibility of environmental risk factors contributing to the cause of ASD. Therefore, identifying potential environmental risk factors relating to development of ASD would be an important research issue as it may help locate avoidable environmental factors and suggest ways of prevention of ASD.

Psychological stress during pregnancy has been considered as one of the environmental risk factors that played a role in development of autism. Such maternal stress as risk factors of ASD have been supported by various kinds of research studies. (Beverdors, Manning, Hillier, Anderson, Nordgren, Walters, Nagaraja, Cooley, Gaelic & Bauman, 2005; Kinney, Miller, Crowley, Huang & Gerber, 2008; Kinney, Munir, Crowley & Miller, 2008; Ward, 1990).

Ward (1990) conducted a retrospective study to compare the presence of family problems during pregnancy between mothers of children with ASD and mothers of normal children. Mothers of autistic children were found to have encountered significantly more family discords and psychiatric problems than those of normal children. However, this study only had considered

family problems as the sources of prenatal stress, other possible sources such as the change of place of residence, unhappiness related to work, financial strain, and sleeping problems during pregnancy were not addressed.

A similar study using complementary survey design by Beversdolf *et al.* (2005) further suggested significantly higher incidence of prenatal stress in mothers of autistic children compared with mothers of normal children and children with Down syndrome. It also found highest incidence of prenatal stress in the 21-32 weeks of gestation. This study made use of the Social Readjustment Rating Scale (SRRS) developed by Holmes & Rahe (1967) as an objective measure on the stress level by different sources of stress. Nevertheless, the same kind of source may result in different intensity of psychological stress for different people as affected by self- perception on the stress. Therefore, subjective rating on the stress level according to the participant's impression may be considered as possible modification of such study.

Apart from survey studies, a natural experiment by Kinney *et al.* (2008) considered hurricanes and tropical storms in Louisiana of America as stressful events experienced by pregnant mother during gestation. The prevalence rate of ASD was found to increase with the severity of prenatal storm exposure. The incidence of ASD was also found to be higher for storm exposure near the middle or end of gestation compared with other time period of gestation.

These three studies all found significant association between prenatal stress and increased risk of ASD. These also provided evidence for specific periods of gestation that are most associated with such risk.

In addition, prenatal stress was found to result in development of various behaviors which were common characteristics in ASD as reported by Kinney *et al.* (2008). A specific brain area called orbitofrontal cortex (OFC), which is responsible for self-regulation of social emotional

behaviors, was found to be sensitive to effects of prenatal stress (Mennes, Stiers, Lagae & Van den Bergh, 2006). Besides, in a study on prenatal exposure to stressful event which considered ice storm as the source of prenatal stress, children with higher prenatal storm exposure were found to demonstrate more stereotypic playing behaviors than those with less storm exposure (King & Laplante, 2005). These indicated prenatal stress was likely to result in development of ASD key features such as impaired social interaction, emotion problems and stereotyped behaviors.

Although the above studies all supported the hypothesis of association between prenatal stress and risk of ASD, this was opposed by a current population-based cohort study in Denmark (Li, Vestergaard, Obel, Christensen, Precht, Lu & Olsen, 2009). Maternal bereavement was considered as the source of prenatal stress and all the singletons born in the period of 1978 to 2003 in Denmark were included in this study. Those with mothers who lost a close relative during pregnancy or up to one year before pregnancy were in the exposed group while the others were in the control group. The rate of onset of autism was compared between these two groups and strong association was not found between prenatal stress from maternal bereavement and the risk of autism. However, this study only considered maternal bereavement as the source of prenatal stress and other sources such as conflicts with family member, unhappiness in work, financial strain were not investigated.

Moreover, all the studies mentioned above were conducted in American or European populations. No related researches on prenatal stress and risk of ASD have been carried out in Chinese population. Therefore, further studies on the relationship between prenatal stress and ASD would be required.

The aim of this paper was to investigate whether there was a positive relationship between the incidence of ASD and the intensity of prenatal stress. The incidences of various sources of

prenatal stress during pregnancy were compared between the mothers of autistic children and the mothers of children with no neurodevelopmental diagnoses. These mothers were interviewed by a survey about the incidence of different stressful events during the gestation period and the perceived intensity of stress. Subjective rating of stress level by the participants was included. This was the first retrospective survey study on the association between prenatal stress and risk of ASD in Chinese population. The findings of the present study would also reveal the following:

1. comparison on findings with other previous researches;
2. clinical implications of the findings;
3. other possible risk factors that may contribute to incidence of ASD apart from prenatal stress;
4. incidence of other possible developmental problems apart from ASD that may correlate with prenatal stress.

Method

Participants

A survey study was carried out to compare the prenatal stresses suffered by two groups of mothers: (1) Twenty-eight mothers of children diagnosed with ASD aged between three to seven years old; (2) Thirty-eight mothers of children with no diagnoses of neurodevelopmental diseases aged between three to seven years old.

Questionnaires (Appendix A: Chinese version; Appendix B: English version) with consent letters (Appendix C) have been distributed through several special child care centres (SCCC), early education and training centres (EETC), and The Society for the Welfare of the Autistic Persons (自閉症人士福利促進會) to parents of children diagnosed with ASD for the data collection on ADS group; and through Sun Island Kindergarten Metro Harbour Branch (太陽島

幼稚園(灣豪庭分校) or directly to parents of children with no history of neurodevelopmental diseases to gather information for the control group.

The consent letters and questionnaires were the same for two groups. Both groups were informed of the purpose of the research as “investigation on relationship between prenatal stress and child developmental health”. The study focus on ASD was not mentioned in the questionnaire so that the interviewees of the ASD group would not relate the questions to the diagnosis of ASD when rating the stress level, and would not try to overrate the level of stress to satisfy the research question.

Procedures

The survey questions were designed based on the sources of stress mentioned in the Social Readjustment Rating Scale (SRRS) (Holmes & Rahe, 1967) and in unpublished articles by Luc (2009). The questionnaire was composed of questions on: (a) background information of the participant’s child; (b) peri-natal and postnatal health conditions; (c) medical complications and developmental problems of the child after birth; (d) maternal age and maternal health conditions; (e) incidence and intensity of psychological stress during pregnancy; (f) coping strategies towards prenatal stress; and (g) the demographic information of the participant.

The level of prenatal stress experienced by the participants was estimated by asking them to recall the stressful events happened during their pregnancies and rate the corresponding stress level. The participants were asked to rate the level of stress caused by different sources, including (i) self-attitude on pregnancy; (ii) spouse’s desire on pregnancy; (iii) change in place of residence; (iv) estrangement or separation from spouse; (v) changes in family dynamic; (vi) conflicts with family members or friends; (vii) death of family members or friends; (viii) illness suffered by family

members or friends; (ix) overwork; (x) working unhappiness; (xi) changes in working conditions; (xii) financial strain; and (xiii) sleeping problems.

The participants were required to rate the stress level by putting a short vertical line onto any point of a “0-100” number line that best represented the level of stress from that corresponding source. The number line was 10cm long with landmarks of “0”, “25”, “50”, “75” or “100” on each 2.5cm interval. A short vertical line towards the left (0) side means there was no stress caused by that factor; while a short vertical line towards the right (100) side means maximum level of stress caused by that factor. The ratings were quantified according to the position of the vertical line in ratio to the landmarks of “0”, “25”, “50”, “75” and “100” on the “0-100” number line. For example, a marking on the 6.4cm position relatively to the 10cm number line would be considered as stress level of 64.

Results

Statistical procedures

Twenty-eight surveys from the ASD group and thirty-eight surveys from the control group were analyzed. Descriptive statistics was used to for comparison between groups in which the data could not be quantified, such as the incidence of medical complications, developmental problems, maternal age, and maternal health condition in each group.

Inferential statistical comparison was carried out between the intensity of prenatal stress of two groups, including both the total stress level, stress level of each individual source of stress and total weighted stress level. Such comparison was also carried out between the ages of participants’ children, and the maternal age of the participants in each group.

Normality test Shapiro-Wiki was used check the presence of normal distribution and hence the qualification of the data for parametric statistical measures. Only normal distribution of data in

both groups of each pair of comparison would be qualified for parametric measures. However, all pairs of comparison were found to fail to meet the criteria of normal distribution for parametric measures. Therefore, non-parametric statistical measures Mann-Whitney test was used for all the inferential statistical comparisons in this study.

Incidence and intensity of prenatal stress

The participants were asked to rate the stress level of thirteen sources of stress: 1. self-attitude on pregnancy; 2. spouse's desire on pregnancy; 3. change in place of residence; 4. estrangement or separation from spouse; 5. change in family dynamic; 6. conflicts with family members or friends; 7. death of family members or friends; 8. illness suffered by family members or friends; 9. overwork; 10. working unhappiness; 11. change in working conditions; 12. financial strain; and 13. sleeping problems. Among all sources, the sources of self-attitude on pregnancy and spouse's desire on pregnancy were present and rated by all the participants. The incidence of other sources of stress was calculated and showed in *Figure 1*.

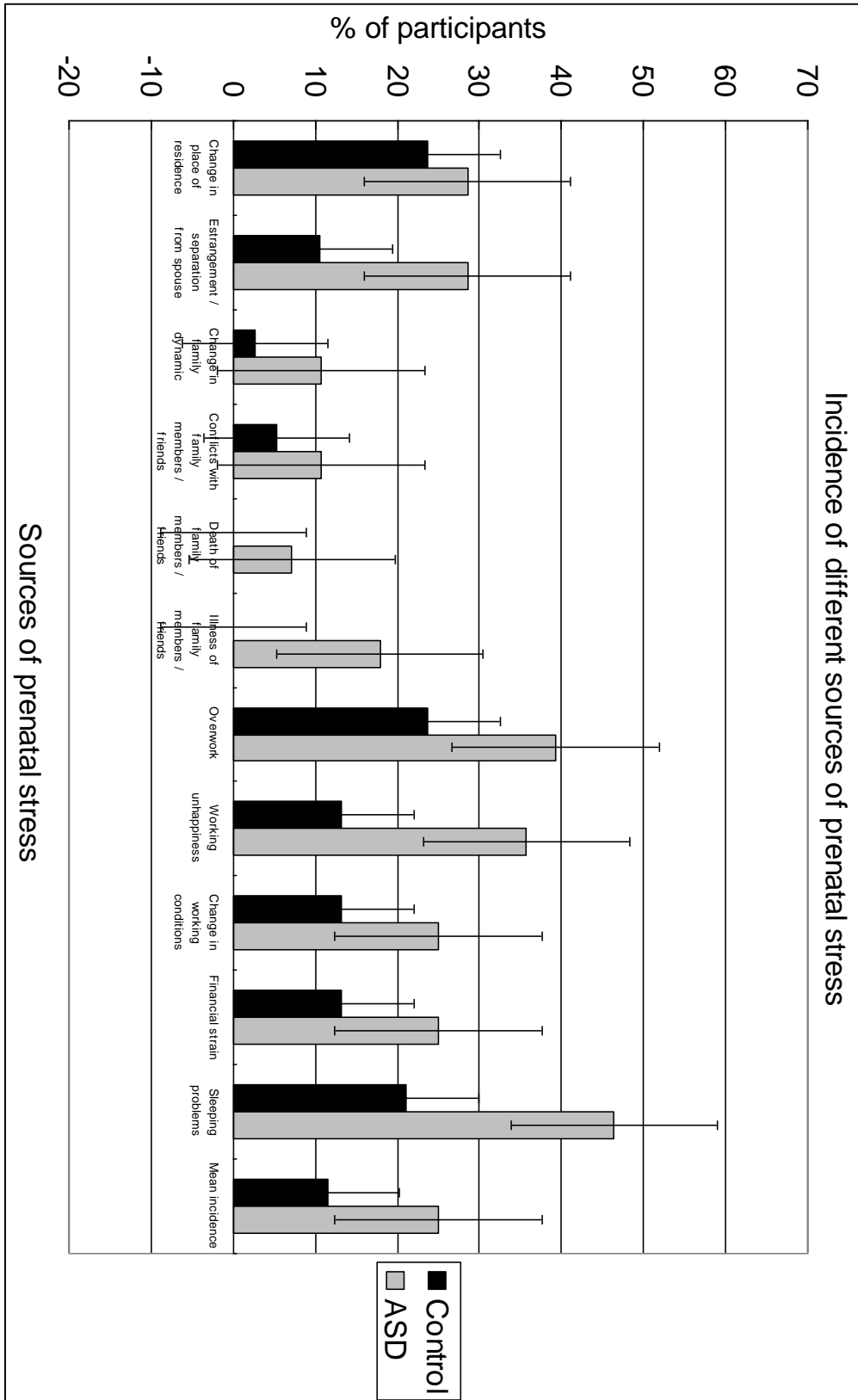


Figure 1. The incidence of different sources of stress

The incidences of all the sources of stress were significantly higher in the ASD group than the control group ($U = 22, p = 0.01$).

Total stress level experienced by each participant was calculated by summing up the stress level of all the sources of stress based on the participant's rating. The mean of the total stress level experienced by the control group was 165.2 (SD = 131.4); while the mean of the total stress experienced by the ASD group was 238.0 (SD = 124.0). The total stress level experienced by each participant was found to be significantly higher in the ASD group ($U = 318.5, p = 0.006$) than in control group.

Some sources of stress were mentioned in the Social Readjustment Rating Scale (SRRS) (Holmes & Rahe, 1967) used by the previous retrospective survey study by Beversdorf et al. (2005), including: change of place of residence; conflicts with family members or friends; death of family members or friends; illness suffered by family members or friends; overworking; working unhappiness; change of working conditions; financial problems; and sleeping problems. A weighted total stress level experienced by each participant was calculated by summing up the stress level of the above stressors based on the estimated stress level mentioned in SRRS. The mean of the weighted total stress level experienced by the control group was 14.62 (SD = 22.13); while the mean of the weighted total stress experienced by the ASD group was 40.52 (SD = 32.70). The weighted total stress level was found to be significantly higher ($U = 261, p < 0.000$) for the ASD group than the control group.

The stress level of each source of stress was also compared between two groups. Those participants reported having no exposure to a particular source of stress were excluded in the comparison of that source. The number of participants was too small for statistical analysis for certain sources of stress that were absent in most participants' gestation period including: change

of family dynamic; death of family members or friends; and illness suffered by family members or friends. The results of the comparison of other sources of stress were summarized in Table 1.

Table 1

Comparison on stress level of different sources of stress between two groups

Source of stress	Control Mean stress level (\pm) SD	ASD Mean stress level (\pm) SD	Significant value of Mann-Whitney U (<i>p</i>)
Self-attitude on pregnancy	48.55 \pm 30.21	29.11 \pm 25.45	0.008
Spouse's desire on pregnancy	45.18 \pm 34.18	35.11 \pm 28.61	0.209
Change in place of residence	43.56 \pm 26.97	47.50 \pm 21.04	0.807
Estrangement / separation from spouse	80.75 \pm 11.30	52.00 \pm 21.76	0.048
Conflicts with family members / friends	60.5 \pm 7.78	78.67 \pm 4.04	0.200
Overwork	60.33 \pm 19.27	68.82 \pm 12.26	0.456
Working unhappiness	54.4 \pm 34.52	76.00 \pm 12.20	0.254
Change in working conditions	45.40 \pm 28.34	72.86 \pm 10.75	0.149
Financial strain	69.80 \pm 36.75	71.43 \pm 17.25	0.639
Sleeping problems	51.00 \pm 22.82	57.15 \pm 22.33	0.422

The stress level of self-attitude on pregnancy, and estrangement or separation from spouse was significantly higher for the control group than the ASD group. No statistical significant difference was found for the stress level of other sources between two groups.

Characteristics of the participants' children

No significant difference was found in age of child between the ASD group and the control group ($U = 484.5, p = 0.52$). Other characteristics of the two groups were listed in Table 2.

Table 2

Characteristics of the studied population

Characteristics	Control	ASD
Age of child /year (mean \pm SD)	4.75 \pm 1.40	4.56 \pm 1.54
Male gender (%)	39.47	82.14
Preterm (%)	5.26	3.57
Low birth weight (%)	5.26	18.86
Birth complications (%):		
Jaundice	5.26	9.29
Cord entanglement	2.63	3.57
Forceps delivery	10.53	17.86
Anoxia	0.00	7.14
Mean	4.61	9.47
Health problems (%):		
Head injury	0.00	10.71
Epilepsy	0.00	21.43
Otitis media	0.00	32.14
Spasm	0.00	3.57
Mean	0.00	16.96
Developmental problems (%):		
Physical handicap	0.00	7.14
Behavioral problems	2.63	39.29
ADHD	0.00	32.14
Language disorders	0.00	85.71
Dyslexia	0.00	14.29
Mean	0.53	35.71

The ASD group got a higher percentage of males. Children born before 37th week of gestation were considered as preterm while those with birth weight less than 2.5 kilograms or 5.5 pounds were considered as having low birth weight (Rais-Bahrami, Short & Batshaw, 2002). The control group showed higher percentage of preterm than ASD group, while the ASD group showed higher percentage of participant's children having low birth weight.

Besides, the children of ASD group showed higher incidence of all kinds of birth complications including jaundice, umbilical cord entanglement, forceps delivery and anoxia than the control group. Health problems such as head injury, epilepsy, otitis media and spasm, were absent in the control group, while 53.57% of the participants in ASD group reported medical history of at least one of the above health problems.

Since one of the subject requirement of the control group was no diagnosis of neurodevelopmental diseases, developmental problems including language disorders, Attention Deficit and Hyperactivity Disorder (ADHD), dyslexia and physical handicap were all absent in the control group. Only 1 participant in the control reported history of behavioral problems of the child. For the ASD group, 85.71% of the participants reported diagnosis of language disorder and about one third of the participants reported diagnosis of ADHD and behavioral problems.

Maternal health and maternal health condition

The distribution of maternal age of the participants in each group was shown in *Figure 2*.

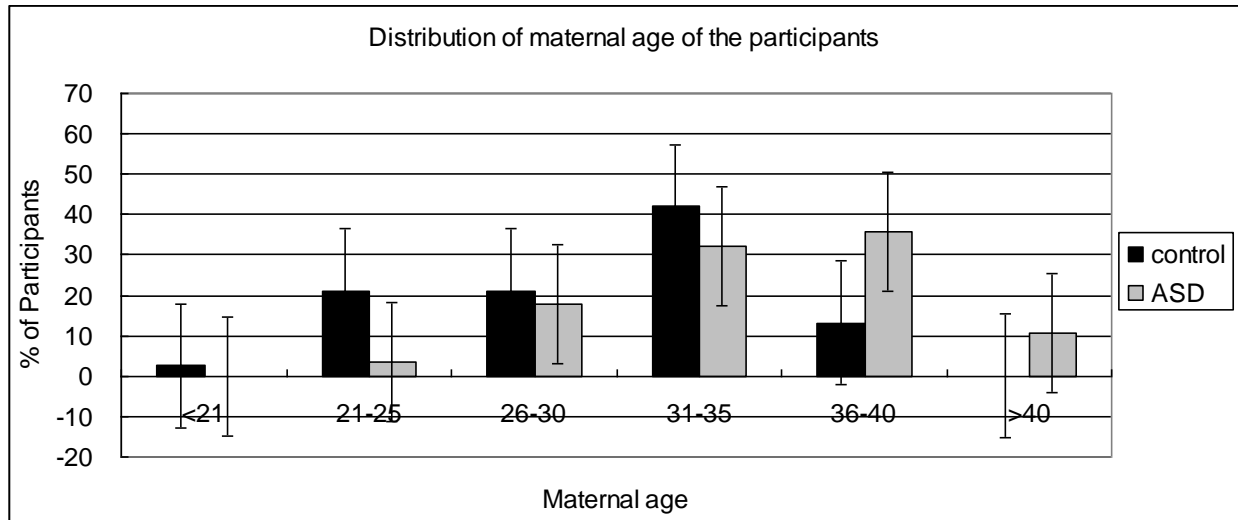


Figure 2. Distribution of maternal age of participants

The mean maternal age of participants in control group was 30.11 while the mean maternal age of the participants in ASD group was 34.61. The maternal age of the participants was found to be significantly higher for the ASD group than the control group ($U=300, p=0.002$)

For the health condition of the participants during pregnancy, the incidences of different factors that were associated with the participant's health in gestation period were listed in Table 3.

Table 3

Incidence of different factors associated with maternal health condition

Factor	% of participants in control group	% of participants in ASD group
Illness	10.53	28.57
Medication	18.42	35.71
Injection	5.26	7.14
X-ray check-up	7.89	3.57
Smoking	2.63	3.57
Drinking	0.00	0.00

The participants in ASD group showed higher incidence of illness, medication, injection and smoking habit during pregnancy, while the control group showed slightly higher incidence of X-ray check-up in gestation period. However, injection, X-ray check-up, and smoking habit were rare for both groups and drinking habit was absent in both groups. Among the 28.57% of participants in the ASD group who reported having diseases during gestation period, 10.7% had cold, but the participants in ASD group still showed higher incidence of the maternal illness hypertension and its related medication.

Coping strategies to relieve prenatal stress by the participants

The frequency of self-coping strategies by each participant to relieve stress during pregnancy, and the frequency of such coping strategies by their spouses were summarized in *Figure3.* and *Figure 4.* respectively.

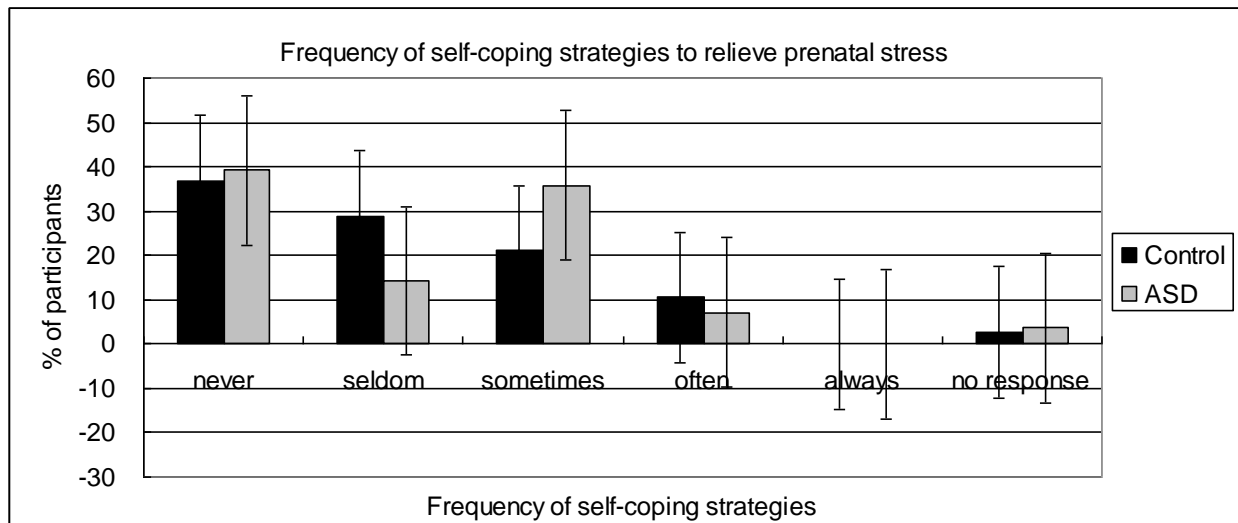


Figure 3. Frequency of self-coping strategies to relieve prenatal stress

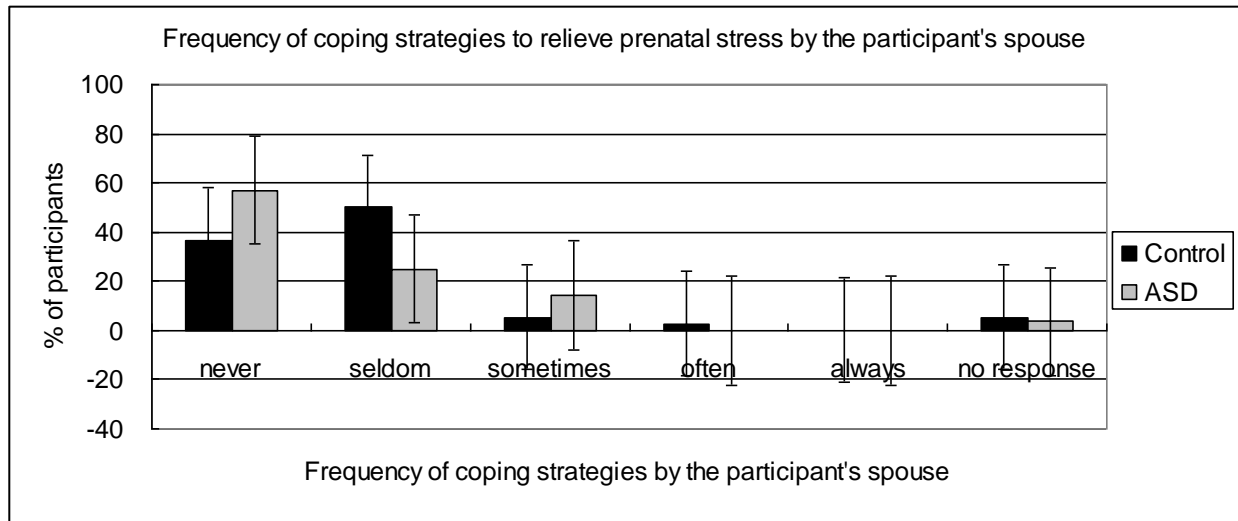


Figure 4. Frequency of coping strategies to relieve prenatal stress by the participant's spouse

Over 80% of the participants in both group (86.84% in control group, 89.39% in ASD group) reported never, seldom or sometimes perform coping strategies to relieve prenatal stress; while over 80% of participants in both group (86.74% in control group, 82.14% in ASD group) reported their spouse only never or seldom demonstrate coping strategies to relieve their stress during pregnancy.

Discussion

Association between prenatal stress and incidence of ASD

The incidences of all the sources of prenatal stress experienced by the participants in ASD group were significantly higher than the control group. This contributed to the significantly higher total stress level in the ASD group than the control group. Moreover, the weighted total stress level of the ASD group was also significantly higher than the control group. It was consistent with the findings of the retrospective survey study by Beversdorf *et al.* (2005) and further supported the findings of higher overall stress level experienced by mothers of ASD children resulted from

their higher chances of exposure to different sources of stress compared with the control group. Therefore, prenatal stress was likely to be a possible risk factor for the incidence of ASD

However, the intensities of most individual sources of stress were found to be not significantly different between two groups. For certain sources including self-attitude on pregnancy, and estrangement or separation from spouse, the corresponding stress levels were significantly higher for the control group than the ASD group. These indicated that the ASD group only had a higher incidence of exposure to different sources of prenatal stress, but not higher intensity of each source of stress. The level of stress by each source might be similar in the two groups. Hence, the overall higher intensity of stress in the ASD group might be mainly the result of the higher frequency of exposure to different sources of prenatal stress instead of the higher intensity of stress by each individual source.

Clinical implications

As prenatal stress was likely to be a risk factor of ASD, avoiding or reducing prenatal stress may be considered as a possible prevention of incidence of ASD. However, in our study most participants in both the ASD group and the control group reported sometimes, seldom or no uses of self-coping strategies to relieve their stress during pregnancy. At the same time, most participants also reported seldom or no attempt by their spouses to relieve their prenatal stress. These indicated general tendency of lack of coping strategies towards prenatal stress by both the pregnant women themselves and their spouses, regardless of whether their children develop ASD.

Therefore, this would be important to enhance the public awareness on prevention and reduction of maternal stress. Development of some stress management training, social resources and other support for the pregnant women to prevent and reduce the effect of prenatal stress would be important as prevention of ASD. More research studies on this area to reinforce the

argument of prenatal stress as risk factor of ASD would also be necessary to convince the public for the importance of such management.

Other possible factors that may contribute to incidence of ASD

Apart from prenatal stress, there were several factors that may contribute to the results. The ASD group showed higher percentage of participants' children having low birth weight than the control group. Risk of neurological, developmental and neurosensory morbidities have been found to be correlated with low birth weight (Ward & McCune, 2002). Thus, such higher incidence of prematurity in the ASD group might be a possible risk factor that contributes to the incidence of ASD.

Besides, the ASD group showed higher percentage of birth complications including jaundice, umbilical cord entanglement, forceps delivery and anoxia than the control group. Among these birth complications, almost 40% of participants in the ASD group reported history of jaundice of their children. Jaundice has been found to be correlated with sensorineural impairments (Ward & McCune, 2002) and such impairments were common for ASD children. Association between ASD and birth complication such as birth trauma was also suggested by some evidences (Towbin, Mauk & Batshaw, 2002). Therefore, jaundice and other birth complications were also the possible risk factors contributing to incidence of ASD.

Moreover, higher percentage of participants in the ASD group reported history of health problems including head injury, epilepsy, otitis media and spasm, which were all absent in the control group. Head injury may result in impairments which are commonly showed by ASD children while epilepsy was found to occur in about 25-30% autistic children (Giovanardi Rossi, Posar, & Parmeggiani, 2000; Tuchman, 2000) as reported by Towbin *et al.* (2002). Hence, such

higher incidence of health problems reported by the ASD group may contribute to the risk of ASD.

The higher incidence of maternal illnesses and medications may also play a role in risk of ASD. The participants of ASD group were found to have higher percentage of maternal illnesses and medications compared with the control group. The ASD participants showed higher incidence for the maternal illness hypertension and its related medication. Such illness may exert some prenatal stress on the participant. It may also increase the risk of prematurity and placental abruption and result in birth complication (Deering & Satin, 2002). Therefore, the higher incidence of maternal illness in ASD group may be a contributing factor to the risk of ASD.

Furthermore, the difference of maternal age between two groups may contribute to the incidence of above factors including prematurity, health problems, birth complications, and maternal illnesses. The maternal age was significantly higher in the ASD group than the control group and might also suggested a trend of advanced maternal age in ASD group. Advanced maternal age was considered as a risk factor of prematurity (Rais-Bahrami *et al.*, 2002). It was also found to be associated with higher risk of maternal illnesses and birth complications. Therefore, it may be another risk factor contributing to incidence of ASD.

Accordingly, the higher incidence of prenatal stress in the ASD group may not be the only factors contributing to the risk of ASD. The higher incidence of prematurity, birth complications, health problems, maternal illnesses, and advanced maternal age in the ASD group may also be the co-factors correlating with the incidence of ASD. Such factors may hinder the effect on the risk of ASD by prenatal stress or reinforce each other to result in manifestation of ASD.

Other possible developmental problems that may correlate with prenatal stress

The ASD group showed high incidence of developmental problems including ADHD, language disorders, dyslexia, behavioral problems and physical handicap compared with the control group. Language disorders, ADHD and behavioral problems were all common developmental problems associated with ASD (Towbin *et al.*, 2002). However, such developmental problems may hinder the effect of prenatal stress on risk of ASD as prenatal stress may also be risk factor of language disorders, ADHD or other developmental problems instead of only associated with ASD. Hence, prenatal stress could only be considered as a possible risk factor for the incidence of ASD and developmental problems commonly showed by ASD children.

Limitations

There were several limitations of our study concerning the number of participants, the research design, and the characteristics of the studied group.

Firstly, the number of subjects in both groups was limited to form normal distribution for parametric statistical analysis. This restricted the statistical comparison between groups to only non-parametric measures and may have reduced the strength of the statistical significance to support the interpretation made. Besides, the limited sample size may also reduce the external validity for the generalization of the results to the whole population. Moreover, the number of subjects was different for the two groups and this may make the two groups less comparable. This also limited the descriptive comparison between two groups to only comparison on the percentage of participants but not the comparison on the exact number of participants. As the size of sample was small, this may allow apparent great difference in percentage by only small difference in number of participants and may make the results misleading.

Secondly, risk of inaccurate recall and response bias by the participants may exist concerning the retrospective nature of the survey study. With a higher incidence of advanced maternal age in the ASD group, this also indicated older current age of the participants. This might result in response bias since younger participants may have better memory in recalling details of the prenatal period compared. Besides, the difference in educational level and other social background may also lead to variation in response bias. Such retrospective survey which relied on the subjective recall by the participants may also make it difficult to investigate if there are possible critical periods of pregnancy that may be most susceptible to the effect by stressors to result in risk of ASD. The effect of stressors may also sustain for variable period of time among different participants. Hence this study could only investigate the incidence of stressor but not the exact duration of stressor, and the method of subjective recall used by such retrospective survey may not be suitable for such further investigation.

Thirdly, there may be a number of factors correlating with of ASD which may hinder the role of prenatal stress in the risk of ASD. As mentioned before, prematurity, birth complications, health problems, maternal hypertension, and advanced maternal age may also be the risk factors of ASD, this study failed to figure out whether prenatal stress could solely result in incidence of ASD; or the diagnosis of ASD was the result of the other risk factors without an effect by the prenatal stress; or the manifestation of ASD would only be resulted with the co-occurrence of all these possible risk factors. Moreover, for the developmental problems that often associated with ASD including language disorders, ADHD and behavioral problems, this study also failed to distinguish between whether prenatal stress correlated with the incidence of ASD, or correlated with the developmental problems that were common for ASD children but not directly affecting the risk of ASD.

Recommendations

Concerning the limitations mentioned before, recommendations for further investigation would focus on the modification on subject recruitment, other possible ways of study apart from survey design, and the possible areas for further investigation.

Firstly, for subject recruitment, the sample size for further study should be larger enough to form normal distribution for parametric statistical uses so that more variety of statistical comparison and thus more convincing statistical comparison can be made. Moreover, in order to study whether prenatal stress was correlated with only ASD, or only with developmental problems associated with ASD, or with both ASD and developmental problems, further studies may consider introducing more subject groups such as subjects with diagnosis with language disorders without ASD, with diagnosis of ADHD without ASD, with diagnoses of both language disorders and ADHD without ASD, or other combinations of target subjects. The subjects with language disorders or ADHD may also have higher incidence of those birth complications, prematurity, health problems and advanced maternal age compared with the normal population. Therefore, this may further balance the effect of higher incidence of those medication complications in the ASD group and modify the subject group to more comparable with the ASD group.

Secondly, since retrospective survey involved subjective recall and might lead to great amount of response bias, further investigation may consider other ways of study. For example, the survey study on prenatal stress level may start before the birth of the children with pregnant women as interviewees. This would have eliminate the inaccuracy of subjective recall, however, would only be possible with very large sample size to obtain enough subjects of children with diagnosis of ASD and would be very time consuming to wait until the children are old enough for

such diagnosis. Further research may also take reference of the study by Kinney *et al.* (2008) which considered natural disasters as a possible prenatal stressor and compared the resultant incidence of ASD in different regions with different intensity of the stressor. In such study, the level of stress could be measured in a more objective way, and the time of occurrence and duration of stressors could also be noted. Such research may not be feasible in Hong Kong as natural disasters are rare in Hong Kong, however, study with such design may be possible in other regions of Chinese population such as China.

Thirdly, for the possible areas of further investigation, these may include studies on whether there is a critical period during pregnancy which is most susceptible to the effect of prenatal stress; the effect of the duration of stressors on incidence of ASD; the changes of physical health of pregnant women by prenatal stress and how it contributes to the development of ASD; and the relationship between the frequency of coping strategies towards prenatal stress and the resultant stress level.

Conclusion

In summary, higher overall stress level resulted from higher incidence of exposure to different sources of prenatal stress was found to be experienced by mothers of ASD children. The ASD group also showed higher incidence of prematurity, birth complications, health problems, maternal illnesses, and advanced maternal age compared with normal population. Moreover, stronger association with developmental problems were also indicated for the ASD group than the control group. Therefore, prenatal stress, prematurity, birth complications, health problems, maternal illnesses and advanced maternal age were all possible risk factors of ASD and the developmental problems commonly showed by ASD children.

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Appendix A**【產前心理壓力及產後兒童健康發展的問卷調查】****第一部份---孩子資料**

1. 你孩子的性別是？ 男 / 女
2. 你孩子的年齡是？ _____
3. 你的孩子是否自然生產？ 順產 / 剖腹
4. 你孩子的出生日期與預產期相差多少天？ _____天
5. 你的孩子是否早產或晚產？ 早產 / 晚產 / 預期生產
6. 你的孩子出生時的體重是？ _____ kg
7. 生產時, 你的孩子有沒有出現以下情況？

臍帶纏頸	<input type="checkbox"/>	缺氧	<input type="checkbox"/>	利用產夾協助生產	<input type="checkbox"/>
黃疸病	<input type="checkbox"/>	其他特別情況: _____			

8. 你的孩子在出生後初期有沒有嚴重傷病紀錄？ 有 / 沒有
若有, 請註明: _____
9. 你的孩子在出生後初期有沒有入醫院或需要留院觀察？ 有 / 沒有
若有, 請註明: _____
10. 你的孩子在出生後有沒有以下健康問題？

腦炎	<input type="checkbox"/>	頭部受傷	<input type="checkbox"/>	痙攣	<input type="checkbox"/>
高熱引致抽搐	<input type="checkbox"/>	腦性麻痺	<input type="checkbox"/>	中耳炎	<input type="checkbox"/>
其他: _____					

11. 你的孩子在出生後有沒有以下發展問題？

聽覺受損	<input type="checkbox"/>	視覺受損	<input type="checkbox"/>	身體弱能	<input type="checkbox"/>
弱智	<input type="checkbox"/>	情緒及行為問題	<input type="checkbox"/>	專注力不足及過度活躍	<input type="checkbox"/>
自閉症	<input type="checkbox"/>	語言發展遲緩/障礙	<input type="checkbox"/>	讀寫困難	<input type="checkbox"/>
其他: _____					

第二部份---懷孕期間的健康狀況

1. 你懷孕時的年齡是?

<21	<input type="checkbox"/>	21-25	<input type="checkbox"/>	26-30	<input type="checkbox"/>
31-35	<input type="checkbox"/>	36-40	<input type="checkbox"/>	>40	<input type="checkbox"/>

2. 你的配偶在你懷孕時的年齡是?

<21	<input type="checkbox"/>	21-25	<input type="checkbox"/>	26-30	<input type="checkbox"/>
31-35	<input type="checkbox"/>	36-40	<input type="checkbox"/>	>40	<input type="checkbox"/>

3. 是否自然懷孕? 是 / 否

4. 你在懷孕期間有沒有曾患病? 有 / 沒有

若有, 請註明是什麼疾病, 發病的時間及持續期間: _____

5. 你在懷孕期間有沒有服食過藥物? 有 / 沒有

若有, 請註明是什麼藥物, 服食的原因, 時間及持續期間: _____

6. 你在懷孕期間有沒有接受過任何注射(例如安胎針)? 有 / 沒有

若有, 請註明是什麼注射, 注射的原因, 時間及持續期間: _____

7. 你在懷孕期間有沒有曾照 X 光? 有 / 沒有

若有, 請註明照 X 光的原因及時間: _____

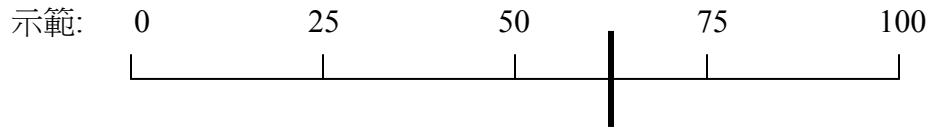
8. 你在懷孕期間有沒有吸煙習慣? 有 / 沒有

9. 你在懷孕期間有沒有飲酒習慣? 有 / 沒有

第三部份---懷孕期間心理狀況

這部份需要你評定懷孕期間各種因素對你的帶來壓力的程度, 請回答以下問題, 並於數線上你認為適當的地方劃上一小直線, 以表示壓力的程度。

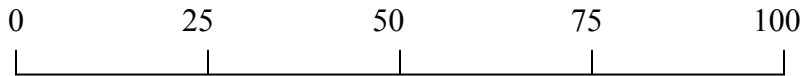
線的左方(0), 代表沒有壓力; 線的右方(100), 代表壓力非常大。



1. 你在懷孕前有生育的計劃嗎? 有 / 沒有

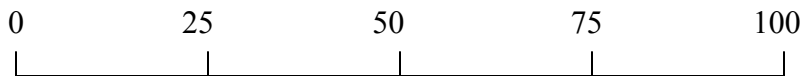
試描述當你知道受孕消息時的感覺: 開心 / 抗拒 / 無奈 / 其他: _____

你認為受孕給予你的壓力程度有多少?



2. 你的丈夫及家人對你的懷孕是否渴求? 是 / 否

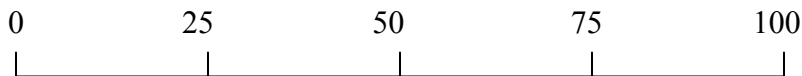
你認為你丈夫或家人對你懷孕的渴求給予你的壓力程度有多少?



3. 你在懷孕期間有沒有轉換過居住地點嗎 (包括遷居, 外出公幹或住院)? 有 / 沒有

若有, 請描述發生的原因, 時間及持續期間: _____

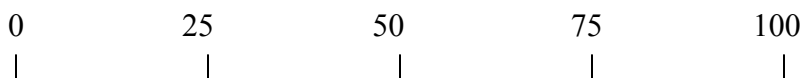
你認為你在懷孕期間轉換居住地點給予你的壓力程度有多少?



4. 你的丈夫在你懷孕期間有沒有離港工作或未能長時間陪伴你? 有 / 沒有

若有, 請描述發生的原因, 時間及持續期間: _____

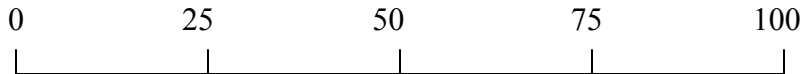
你認為你丈夫在你懷孕期間離港工作或未能長時間陪伴你給予你的壓力程度有多少?



5. 你在懷孕期間有沒有遇到家庭環境變動 (例如: 同住家庭成員數目增加或減少, 分居, 離婚)? 有 / 沒有

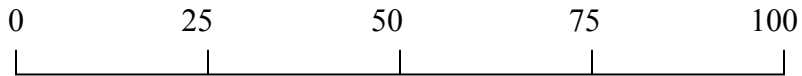
若有, 請描述發生的原因, 時間及持續期間: _____

你認為在你懷孕期間遇到的家庭環境變動給予你的壓力程度有多少？



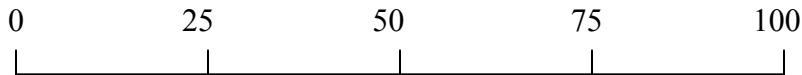
6. 你在懷孕期間與家人, 朋友或工作伙伴有發生過衝突嗎? 有 / 沒有
若有, 請描述發生的原因, 時間及持續期間: _____

你認為你在懷孕期間與家人或朋友發生的衝突給予你的壓力程度有多少?



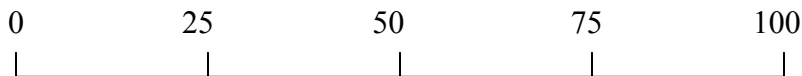
7. 在你懷孕期間有親人或好友離逝或遇到意外嗎? 有 / 沒有
若有, 請描述發生的原因及時間: _____

你認為在你懷孕期間你親人或好友的離逝或意外給予你的壓力程度有多少?



8. 在你懷孕期間, 你或你的親人或好友有患病嗎? 有 / 沒有
若有, 請描述發生的情況, 時間及持續期間: _____

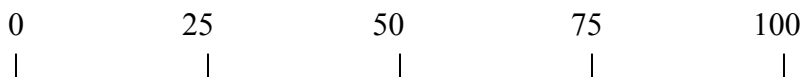
你認為在你懷孕期間你或你的親人或好友患病給予你的壓力程度有多少?



9. 你在懷孕期間有沒有工作過度嗎? 有 / 沒有

若有, 請描述工作過度的情況, 發生時間及持續期間: _____

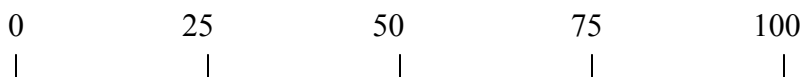
你認為在你懷孕期間遇到工作過度給予你的壓力程度有多少?



10. 你在懷孕期間有沒有在工作上遇到不快的事? 有 / 沒有

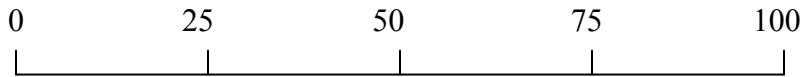
若有, 請描述事件的情況, 發生時間及持續期間: _____

你認為在你懷孕期間在工作上遇到的不快事給予你的壓力程度有多少?



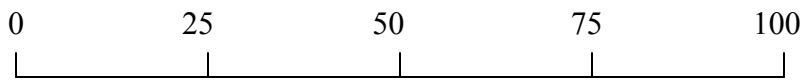
11. 你在懷孕期間有否遇到工作環境變動或人事變動 (例如: 升職, 降職, 調職, 被解僱, 工作伙伴變動, 工作環境轉變, 工作時間變動)? 有 / 沒有
若有, 請描述變動的情況, 發生時間及持續期間: _____

你認為在你懷孕期間遇到的工作上人事變動給予你的壓力程度有多少?



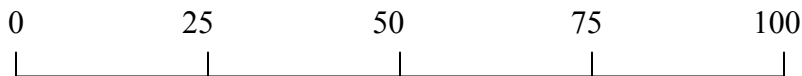
12. 你在懷孕期間有否遇到財政困難? 有 / 沒有
若有, 請描述困難的情況, 發生時間及持續期間: _____

你認為在你懷孕期間遇到的財政困難給予你的壓力程度有多少?



13. 你在懷孕期間有否失眠問題? 有 / 沒有
若有, 請描述失眠的情況, 發生時間及持續期間: _____

你認為在你懷孕期間遇到的失眠問題給予你的壓力程度有多少?



第四部份--處理產前壓力的方法

1. 你曾嘗試尋找減壓方法以舒緩懷孕期間遇到的壓力嗎?
從不 / 很少 / 有時 / 很多時 / 總是
若有, 請註明是什麼方法: _____
你認為這些減壓方法有效嗎?
非常不有效 / 不有效 / 一般有效 / 很有效 / 非常有效
請描述這些減壓方法對你的心理狀況有什麼影響: _____

2. 你的丈夫及其他家人曾嘗試尋找減壓方法以舒緩你懷孕期間遇到的壓力嗎?
從不 / 很少 / 有時 / 很多時 / 總是
若有, 請註明是什麼方法: _____
你認為這些減壓方法有效嗎?
非常不有效 / 不有效 / 一般有效 / 很有效 / 非常有效
請描述這些減壓方法對你的心理狀況有什麼影響: _____

第五部份---基本資料

請回答以下有關你個人資料的問題。

1. 年齡

<21	<input type="checkbox"/>	21-25	<input type="checkbox"/>	26-30	<input type="checkbox"/>
31-35	<input type="checkbox"/>	36-40	<input type="checkbox"/>	41-45	<input type="checkbox"/>
46-50	<input type="checkbox"/>	50-55	<input type="checkbox"/>	>55	<input type="checkbox"/>

2. 職業

銀行 <input type="checkbox"/>	會計 <input type="checkbox"/>	電腦 <input type="checkbox"/>
飲食 <input type="checkbox"/>	文員 <input type="checkbox"/>	時裝 <input type="checkbox"/>
教育 <input type="checkbox"/>	酒店 <input type="checkbox"/>	社工 <input type="checkbox"/>
家庭主婦 <input type="checkbox"/>	工程 <input type="checkbox"/>	其他: _____

3. 教育程度

小學或以下 <input type="checkbox"/>	中學 <input type="checkbox"/>
文憑 / 高級文憑 / 副學士 <input type="checkbox"/>	大學或以上 <input type="checkbox"/>

4. 家庭每月收入

< \$5,000 <input type="checkbox"/>	\$5,000 - \$9,999 <input type="checkbox"/>	\$10,000 - \$14,999 <input type="checkbox"/>
\$15,000-19999 <input type="checkbox"/>	\$20,000 - \$24,999 <input type="checkbox"/>	\$25,000 - \$29,999 <input type="checkbox"/>
\$30,000 - \$34,999 <input type="checkbox"/>	\$35,000 - \$49,999 <input type="checkbox"/>	50,000> <input type="checkbox"/>

~謝謝你的參與~

Appendix B

[A survey study on prenatal stress and postnatal child health development]

Part 1---Child information

1. Gender of your child: male / female

2. Age of your child: _____

3. Was your child born through natural labour? Natural labour / Operation

4. What was the time difference between the date of birth of your child and the expected birthday?
_____ days

5. Was your child born as premature? Yes / No

6. What was the birth weight of your child? _____ kg

7. Were there any birth complications? Yes / No

If yes, please specify:

Cord entanglement <input type="checkbox"/>	Anoxia <input type="checkbox"/>	Forceps delivery <input type="checkbox"/>
Jaundice <input type="checkbox"/>	Others: _____	

8. Did your child experience any severe postnatal impairment soon after birth? Yes / No

If yes, please specify: _____

9. Did your child stay in hospital for observation for a period of time during the postnatal period?

Yes / No

If yes, please specify: _____

10. Does your child have the following health problems?

Encephalitis <input type="checkbox"/>	Head injury <input type="checkbox"/>	Spasm <input type="checkbox"/>
Epilepsy <input type="checkbox"/>	Cerebral palsy <input type="checkbox"/>	Otitis media <input type="checkbox"/>
Others: _____		

11. Does your child have the following development problems?

Hearing impairment <input type="checkbox"/>	Visual impairment <input type="checkbox"/>	Physical handicap <input type="checkbox"/>
Mental retardation <input type="checkbox"/>	Emotional or behavioral problems <input type="checkbox"/>	Attention-deficit and hyperactivity disorder (ADHD) <input type="checkbox"/>
Autism Spectrum Disorder (ASD) <input type="checkbox"/>	Language delay/disorder <input type="checkbox"/>	Dyslexia <input type="checkbox"/>
Others: _____		

Part 2---Maternal health conditions

2. How old were you when you became pregnant?

<21	<input type="checkbox"/>	21-25	<input type="checkbox"/>	26-30	<input type="checkbox"/>
31-35	<input type="checkbox"/>	36-40	<input type="checkbox"/>	>40	<input type="checkbox"/>

2. How old was your spouse when you became pregnant?

<21	<input type="checkbox"/>	21-25	<input type="checkbox"/>	26-30	<input type="checkbox"/>
31-35	<input type="checkbox"/>	36-40	<input type="checkbox"/>	>40	<input type="checkbox"/>

3. Was the pregnancy naturally developed? Yes / No

4. Did you get any health problems or diseases during pregnancy? Yes / No
If yes, please specify the nature of disease, time and duration of incidence:

5. Did you take any medication during pregnancy? Yes / No
If yes, please specify the nature of medicines, time and duration of consumption:

6. Did you receive any injection during pregnancy? Yes / No
If yes, please specify the nature of injection, time and duration of injection:

7. Did you receive any X-ray check up during pregnancy? Yes / No
If yes, please specify the reason and time of X-ray check up:

8. Did you have smoking habit during pregnancy? Yes / No

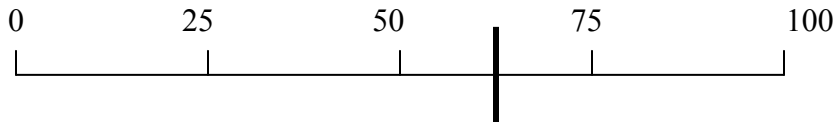
9. Did you have alcohol drinking habit during pregnancy? Yes / No

Part 3---Prenatal psychological conditions

This part requires your rating on the level of stress arisen from different factors during your gestation period. Please answer the following questions, and put a short vertical line onto any point of the number line that best represents the stress level.

A short vertical line towards the left (0) side means there was no stress caused by that factor; while a short vertical line towards the right (100) side means maximum level of stress was caused by that factor.

Demonstration:

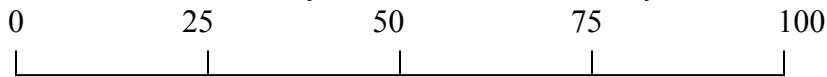


1. Was the pregnancy planned? Yes / No

Please describe your feeling when you were informed getting pregnant:

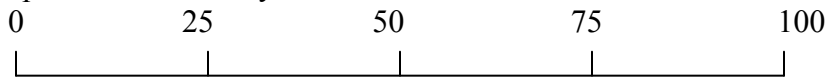
Happy / Reluctant / Confused / Others: _____

What was the level of stress you think was arisen from your attitude on pregnancy?



2. Was the pregnancy desired by your spouse and/or family? Yes / No

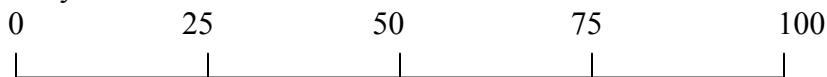
What was the level of stress you think was arisen from the desire towards your pregnancy by your spouse and/or family?



3. Did you experience any changes in place of residence during pregnancy? (e.g. changing residence, trip, or staying in hospital, etc.)? Yes / No

If yes, please specify the condition, time and duration of incidence:

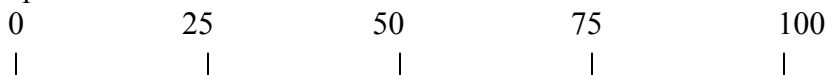
 What was the level of stress you think was arisen from the change in place of residence during pregnancy?



4. Did you experience any estrangement or separation from your spouse during pregnancy? (e.g. you partner was working all the time or travel for his work, etc.)? Yes / No

If yes, please specify the condition, time and duration of separation:

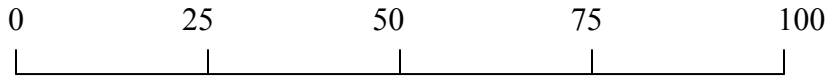
 What was the level of stress you think was arisen from the estrangement or separation from your spouse?



5. Did you experience any change in family dynamic during pregnancy? (e.g. increasing number of family members, divorce, etc.)? Yes / No

If yes, please specify the condition, time and duration of incidence:

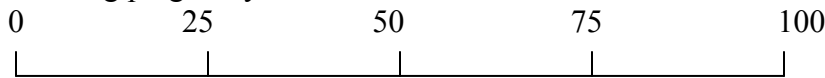
What was the level of stress you think was arisen from the change in family dynamic during pregnancy?



6. Did you experience any conflicts with your family, friends or working partners during pregnancy? Yes / No

If yes, please specify the condition, time and duration of incidence:

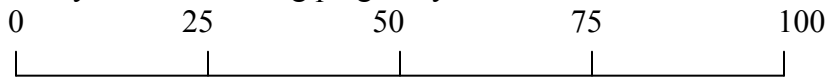
What was the level of stress you think was arisen from the conflicts with your family or friends during pregnancy?



7. Did you experience any bad news on death or accident of your family or friends during pregnancy? Yes / No

If yes, please specify the condition, time and duration of incidence:

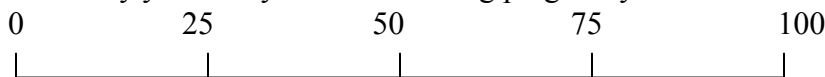
What was the level of stress you think was arisen from the bad news on death or accident of your family or friends during pregnancy?



8. Did you experience any illness or have your family or friends experienced any illness during your pregnancy? Yes / No

If yes, please specify the condition, time and duration of incidence:

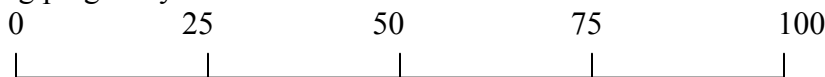
What was the level of stress you think was arisen from the illness you experienced or experienced by you family or friends during pregnancy?



9. Did you experience physical and/or mental overwork during pregnancy? Yes / No

If yes, please specify the condition, time and duration of incidence:

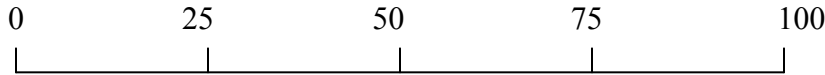
What was the level of stress you think was arisen from the physical and/or mental overwork during pregnancy?



10. Did you experience any unhappiness related to work during pregnancy? Yes / No

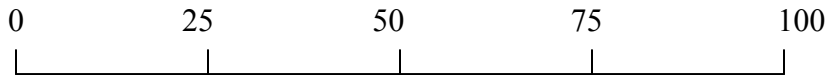
If yes, please specify the condition, time and duration of incidence:

What was the level of stress you think was arisen from the unhappiness related to work during pregnancy?



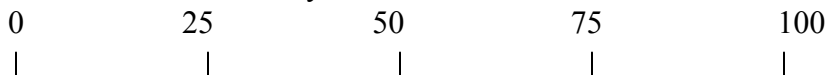
11. Did you experience any changes in working conditions (e.g. changes in working position, changes in working partners, being fired, etc.) during pregnancy? Yes / No
If yes, please specify the condition, time and duration of incidence:

What was the level of stress you think was arisen from the changes in working conditions during pregnancy?



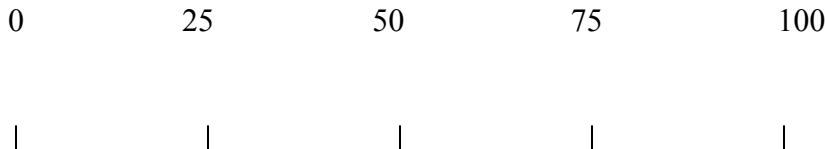
12. Did you experience any financial strain during pregnancy? Yes / No
If yes, please specify the condition, time and duration of incidence:

What was the level of stress you think was arisen from the financial strain during pregnancy?



13. Did you experience any sleeping problems during pregnancy? Yes / No
If yes, please specify the condition, time and duration of incidence:

What was the level of stress you think was arisen from the sleeping problems during pregnancy?



Part 4---Coping strategies for prenatal stress

3. Have you tried any strategies in relieving the prenatal stress you faced?
Never / Seldom / Sometimes / Often / Always

If yes, what were your strategies: _____

Were the strategies effective?

Very ineffective / ineffective / generally effective / quite effective / very effective

Please describe how these strategies affected your psychological condition:

4. Have your spouse or other family members tried any strategies in relieving the prenatal stress you faced?

Never / Seldom / Sometimes / Often / Always

If yes, what were your strategies: _____

Were the strategies effective?

Very ineffective / ineffective / generally effective / quite effective / very effective

Please describe how these strategies affected your psychological condition:

Part 5---Basic information

Please answer the following questions about your basic information.

1. Age

<21	<input type="checkbox"/>	21-25	<input type="checkbox"/>	26-30	<input type="checkbox"/>
31-35	<input type="checkbox"/>	36-40	<input type="checkbox"/>	41-45	<input type="checkbox"/>
46-50	<input type="checkbox"/>	50-55	<input type="checkbox"/>	>55	<input type="checkbox"/>

2. Occupation

Banking	<input type="checkbox"/>	Accounting	<input type="checkbox"/>	Computer related	<input type="checkbox"/>
Catering	<input type="checkbox"/>	Clerk	<input type="checkbox"/>	Fashion related	<input type="checkbox"/>
Education	<input type="checkbox"/>	Hotel related	<input type="checkbox"/>	Social worker	<input type="checkbox"/>
Housewife	<input type="checkbox"/>	Engineering	<input type="checkbox"/>	Others: _____	

3. Educational level

Primary school or below	<input type="checkbox"/>	Secondary school	<input type="checkbox"/>
Diploma / High Diploma / Associate Degree	<input type="checkbox"/>	Bachelor Degree or above	<input type="checkbox"/>

4. Family income per month

< \$5,000	<input type="checkbox"/>	\$5,000 - \$9,999	<input type="checkbox"/>	\$10,000 - \$14,999	<input type="checkbox"/>
\$15,000-19,999	<input type="checkbox"/>	\$20,000 - \$24,999	<input type="checkbox"/>	\$25,000 - \$29,999	<input type="checkbox"/>
\$30,000 - \$34,999	<input type="checkbox"/>	\$35,000 - \$49,999	<input type="checkbox"/>	50,000>	<input type="checkbox"/>

~ Thank you for your participation.~

Appendix C**參加者研究者同意書 INFORMED CONSENT FORM****「產前心理壓力及產後兒童健康發展」研究****A survey study on prenatal stress and postnatal child health development**

香港大學 — 言語及聽覺科學部誠意邀請閣下參與一項由薛安博士主理，名為「產前心理壓力及產後兒童健康發展」的研究。

You are invited to participate in a research study entitled “A survey study on prenatal stress and postnatal child health development” conducted by Dr. Steve Xue in the Division of Speech & Hearing Sciences at the University of Hong Kong.

研究目的 PURPOSE OF THE STUDY

研究目的是為找出產前心理壓力和產後兒童健康發展的關係。

This study aims to find out the relationship between prenatal stress and postnatal child health development.

研究程序 PROCEDURES

是次研究包括一份六頁的問卷調查。所有參加者需要完成該份問卷所有問題，而填寫需時約15分鐘。

The study will involve a 6-page questionnaire. All participants will have to answer all questions of the questionnaire. The whole procedure will take you about 15 minutes.

潛在風險 POTENTIAL RISKS / DISCOMFORTS AND THEIR MINIMIZATION

沒有潛在風險。

No potential risks or discomforts.

研究裨益 POTENTIAL BENEFITS

是次研究並不會為閣下提供直接得益，但是項研究結果將用作日後預防兒童健康發展問題之理據，所以你的參與，將對日後研究有極大的貢獻。

There are no direct benefits to you. However, the research project can provide valuable information on the causes of child developmental health problems. This information in turn could help inform future prevention of these problems.

個人私隱 CONFIDENTIALITY

閣下向研究人員所提供及收集的資料，只供作研究用途，個人資料將絕對保密。閣下的所有資料將以代碼記錄，以保障閣下的私隱。參加者的身份亦不會被公開。

Any information obtained in this study will remain very strictly confidential, will be known to no-one, and will be used for research purposes only. Codes, not names, are used on all subject files to protect confidentiality. Participant will not be identified by name in any report of the completed study.

資料儲存 STORAGE OF DATA

閣下的所提供的資料會透過問卷被記錄及作日後數據複核，儲存資料並不包括閣下的個人資料。所有研究紀錄將會貯存並不會刪除，而有關資料將會被妥善貯放於研究負責人辦公室貯物櫃內並鎖上；而只有研究人員才能取得有關資料。

For research purposes, the information you provided will be recorded through questionnaire for further data checking. The questionnaire will be kept indefinitely. It will be stored in a locked cabinet in the office of the investigator indefinitely. Only the research team will have access to the data.

參與及退出 PARTICIPATION AND WITHDRAWAL

是次研究的參與純屬自願性質，閣下可隨時看研究紀錄，閣下也可隨時提出終止參與此研究，有關決定將不會引致任何不良後果。如有需要，閣下可要求銷毀測試結果。

Your participation in this research study is voluntary. This means that you can choose to withdraw from this project at any time, for any reasons, without negative consequences. We will erase the entire information obtained, or parts of it if you want us to do so.

疑問 QUESTIONS AND CONCERNS

閣下需填寫及簽署一份同意書。如你對是項研究有任何疑問，請現在提出。如日後你對是項研究有任何查詢，敬請聯絡香港大學言語及聽覺科學部助理教授薛安博士 (地址: 菲臘牙科醫院五樓, 電話: 28590581, 電郵: axue@hku.hk) 或研究員鄭欣祺(電話: 90285790, 電郵: janetcyk@gmail.com)。如你想知道更多有關研究參與者的權益，敬請聯絡香港大學非臨床研究操守委員會 (電話: 22415267)。

You will be asked to complete and sign the consent form on the opposite page. If you have any questions or concerns about this research study, please feel free to contact Dr. Steve Xue (Address: 5/F Prince Philip Dental Hospital, The University of Hong Kong; Telephone: 28590581; Email: axue@hku.hk) Associate Professor of Division of Speech and Hearing science, The university of Hong Kong, or the investigator Cheng Yan Ki (Tel: 90285790; E-mail: janetcyk@gmail.com). If you have any questions about your rights as a research participant, please contact the Human Research Ethics Committee for Non-Clinical Faculties, the University of Hong Kong (Tel: 22415267).

我們在此多謝你的參與。

We thank you for your interest and support.

簽署 SIGNATURE

本人 _____ (姓名) 已有足夠機會詢問清楚明白有關這項研究的內容，並同意參加這項研究。

I _____ (Name of Participant) have been given the opportunity to ask questions about this study and they have been answered to my satisfaction. I understand the procedures described above and agree to participate in this study.

參加者姓名(正楷) Name of participant (Block letter)

參加者簽署 Signature of participant