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STATISTIC ANALYSIS ON RELEVANCY OF SCREENING FACTORS IN DOWN'S SYNDROME

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ABSTRACT

The aim of this paper is to analyze the impacts of the pregnant women's ages and the gestational weeks on the serological prenatal screening in Down's syndrome, and then explore and identify the best range of the ages of the pregnant women and the gestational weeks. During 2009 to 2011, there are 3162 pregnant women who had accepted to receive the screening of Down's syndrome, giving the birth in the hospital and being interviewed in Tangshan. During the week fifteenth to the week twenty-first, examine the typical factors of maternal serum, AFP and β-HCG, through the risk evaluation software of Down's syndrome. For the high risk case, the amnionic paracentesis is required for diagnosis. Compare the high risk rate of Down's syndrome between the different groups in different ages. The results of the high risk rate of Down's syndrome got from the different gestational weeks and the false rate of the screening are also needed to be examined. The obtained results can help to improve the accurate rate of the diagnosis, meanwhile reducing the rate of misdiagnosis.

Keywords: *Down's Syndrome, Prenatal Screening, Serological Screening, Statistic Analysis of Affecting Factors*

1. INTRODUCTION

Down's syndrome, Chromosome 21, is one of the commonest birth defect diseases, which is resulted from the Chromosomal Aberration. This disease is due to the birth defect, representing as the intelligent defect. The rate of Chromosome 21 is 1/800～1/600 among the born babies [7]. The clinical representations of this disease are intelligent defect, the hesitating physical growing and abnormal facial appearance, and even congenital heart defect as well as organ malformations accompanying with more than 50% patients. Once the children were born with this disease, it would lead to heavy mental and economical burden on the patients' families and the society [1]. Until now, there is no effective and exact treatment to get over it, so the prenatal screening and diagnosis become obviously significant. The prenatal screening of Down's syndrome as one of the screening methods to ensure the Eugenics, that is, identify the high risk group and then process the diagnosing examine. It is an efficient way to prevent the born of children who are with Down's syndrome [5, 9].

Maternal serum markers for prenatal screening of Down's syndrome is a kind of screening for pregnant women and fetal all non-invasive inspection, simple and convenient method for its economic, high rate, at the same time, also call screen a neural tube defect. Laboratory screening has become the focus of research [2].

2. THEORIES AND APPROACHES

2.1 Theories

From the week fifteenth to the week twenty-first, examine the typical factors of serum, that is, AFP and β-HCG, combining the factors, like age, weight and pregnant weeks and so on all together, and then evaluate the data by the risk evaluation software of Down's syndrome, and finally get the risk rate. When the value of the risk rate is equal to or higher than 1 / 300, it would belong to the high risk group [4].

Exposed rate = true positive rate ÷ the total number of the pregnant women screened (1)

In this index, the higher the exposed rate, the lower false positive rate will be received. It means the better effect of screening examines.

True positive rate (TPR), also called sensitivity, is the rate that the patient is correctly diagnosed and the result is positive. Namely, TPR= the true number of the positive ÷ the true number of the positive = the true number of the positive ÷ the number of the normal. False positive rate (FPR),

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also called the rate of misdiagnosis, is the rate that the patient is wrongly diagnosed and result is also positive, namely,

FPR= the rate of misdiagnosis= the false number of the positive ÷ the number of the healthy= （the number of the positive — the diagnosed number of the positive）÷ (the total number screened — the diagnosed number of the positive) (2)

A multiple of the median（MoM）is a measure to describe how far an individual test result deviates from the median. The application of MoM is helpful to avoid the systematic bias from the difference of the lab, and meanwhile it is able to process the standard screening procedure on the pregnant women. Due to MoM not affected by the external incidental factors, the average value usually does not be adopted. MoM is particularly suitable to be applied into situation that the test index is varying from the factors, such as the age, sex and so on. One reason is due to its sample calculating process, and another reason is that it can eliminate the impact of the units. The most essential one is that it can apparently display the result [4]. Free β-HCG's reference is 0.44~2.42 MoM， AFP's reference is 0.61~2.63[9].

2.2 Approaches

Take down all the factors related screening, such as the occupation, age, weight, the date of last menses, the genetic history, the birth of defect, the medical history of pregnancy and so on.

The main text index: the double markers screening processes on AFP and the concentration of β-HCG. With the risk evaluation software of Down's syndrome, calculate the risk rate of giving a birth of child with Down's syndrome.

Criteria: the threshold of the risk rate is 1：300; if the risk rate is equal to or higher than 1：300, the pregnant women will be diagnosed as the member of the high risk group. Since the screening is not completely equal to the diagnosis, some false results exist; therefore it is necessary to recommend the pregnant women who belong to the high risk group to accept the amnionic paracentesis ，in order to get the child's cell to process the karyotype analysis and then come to the diagnosis. For the pregnant woman who has been diagnosed with Down's syndrome, it ought to be informed to the patient and recommend ceasing the pregnancy.

Specimen's collection and preservation: extract the venous blood (3-5ml), and after separate the serum from the solidified blood, part of the specimen being persevered in the fridge (-20℃). The entire specimen will be collected by the staff of the screening centre in one week. Test AFP and β-HCG with time-resolved fluoroimmunoassay (TRFIA). The other part will be persevered in the fridge (-80℃) for another test.

Statistic analysis: AFP and β-HCG of the pregnant woman's serum are represented and illustrated by MoM, the data being processed and analyzed by EXCEL. The comparison of the risk rate between the pregnant women with the different ages and pregnant weeks is processed by the χ^2 test, and when the value of P is less than 0.05, the difference has the statistic value.

3. THE ANALYSIS OF MATERIAL

3.1 Material

From January to December in 2010, there are 3162 pregnant women (pregnant week is from 15^{+0} to 20^{+6}) received screening, that is, AFT and the concentration of β-HCG going through χ^2 test. The details of the screening are illustrated in the table below: there are 216 pregnant women in the high risk group, so the positive rate is 6.83%; the diagnosis rate is based on the triple analyte screening. The screened high risk pregnant women have accepted the amnionic paracentesis, four of them diagnosed with Down's syndrome; the false negative rate is 6.71%.

Table 1 : The Data Of Different Ages

Age(year)	Total Number	Positive Number
18-20	33	0
20-25	1170	27
25-30	1512	81
30-35	330	81
≥35	117	27
sum	3162	216

3.2 The Statistic Analysis Of The Relevancy Of The Screening Factors

3.2.1 The impact of the age of the pregnancy on screening result of Down's syndrome

In the group the youngest pregnant woman is 18 years, while the oldest is 39 years. The average age is 24.67 years, the standard deviation is 6.16, the value of MoM is 27 years and the pregnant women more 30 years take 14.14%.

According to the screening result of AFT and the concentration of β-HCG going through χ^2 test, there is no pregnant women in the high risk group between age 18 to 20; from age 20 to 25, the selective rate is 2.31%; from age 25 to 30, the selective rate is 5.36%; from age 30 to 35, the selective rate is 24.55%; equal to or more than 35 years, the selective rate is 23.08%. Based on the

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data above, it is obvious that the risk of Down's syndrome is increasing with the growing of the age [8]. For a long time, in China the pregnancy is equal to or more than 35 years that is regarded as one main index to diagnose the Down's syndrome, but in fact it is not absolute. According to the table 1, the high risk group has the following features: as the age is growing, the risk of Down's syndrome is up; however, the highest risk rate appeared in the group aged 30 to 35, nearly 25%. Therefore, the range of the high risk group ought to contain the pregnant women aged equal to or older than 30 years, and at the same time it is.

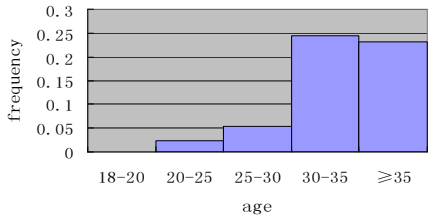

Figure 1: The Relation Of The Pregnant Women's Age And The Risk Rate

3.2.2 The impact of pregnant week on the screening result of Down's syndrome

Due to rare pregnant women aged from 18 to 20 as well as one aged equal to or older than 35 years, they are divided into the group aged 20 to 25 and the group aged 30 to 35 respectively(illustrated in table1 and table 2). According to the table 2, the risk rate of week 16 to week 19 is apparently lower than week 15 to week 20(P<0.05); the risk rate of pregnant women aged from 18 to 30 is obviously lower the one aged older than 30 years (P<0.05). from table 3, the false positive rate of the pregnant week 16 to week 19 (1.30 % ～ 14.29%) is comparatively satisfied; particularly the false positive rate of the pregnant week 16 to week 18 is the best one （1.30%-8.79%）; however, the higher false positive rate is got during the pregnant week 15 and the week 20, and comparing with the others screening result, significant difference can be found (P<0.05).

Table 2: The Data Of Different Ages And Pregnant Week's （一）

Age	Pregnant Week and the High Risk Rate					
(year)	15W	16W	17W	18W	19W	20W
18-25	4.00	3.17	3.00	4.05	3.10	17.39
25-30	18.18	8.79	4.95	5.00	5.36	14.29
≥30	22.73	8.51	1.30	6.45	14.29	25.00

Table 3: The Data Of Different Ages And Pregnant Week's （二）

Age	Pregnant Week and the False Positive Rate					
(year)	15W	16W	17W	18W	19W	20W
18-25	4.00	3.08	3.00	4.05	3.10	17.39
25-30	18.18	8.79	4.90	4.96	5.36	14.29
≥30	22.73	8.51	1.30	6.32	14.29	25.00

3.2.3 The analysis of the relevancy of AFP, β-HCG and pregnant weeks

The serological indexes, AFP and β-HCG, are close to the length of pregnancy, and meanwhile the value of the index also varies from the length of pregnancy[6]. Based on the collected data, the graph illustrates the relationship between the value of the MoM of serological indexes (AFP and β-HCG) and Pregnant weeks (Figure.2).

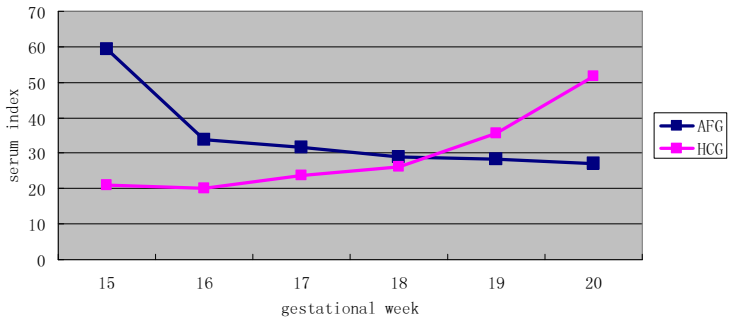

Figure 2: The Relationship Between the High Risk Pregnant Women's AFP And B- HCG And The Pregnant Weeks

It can be seen from the graph that with the growing of the pregnant weeks, the serological index, AFP, is decreasing, while the other index, β-HCG, is increasing[8]. In the normal situation, the serological index, AFP, is increasing with the growing of the pregnant weeks, while the other index, β-HCG, is decreasing.

3.2.4 The Impact of Other Factors on the Serological Indexes

According to the report, there are many factors could affect the screening result, such as race, weight, bad habits(like smoking and drinking), dependent diabetes mellitus, multiple pregnancy and so on[3]. Represented by the studies, as the

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weight grows, the serological indexes, AFP and β-HCG decrease. For the pregnancy with type 1 diabetes mellitus, averagely AFP will decrease 20%; for the smoker, it will decrease 20%-30%. Consequently, if apply the serological indexes into the prenatal screening, other factors affected the positive rate should be took into account[2].

4. CONCLUSION

1. The occurrence of Down's syndrome is closely related to the age of the pregnancy, and with the growth of the age, the positive rate will be up consistently. In our nation, before, the pregnancy is equal to or more than 35 years that is regarded as one main index to diagnose the Down's syndrome. In fact, according to the data, the pregnancy, more than 30 years, should be regarded as one main index to diagnose the Down's syndrome.

2. The serological index, AFP, of the pregnancy in the high risk group, the serological index, HCG, is decreasing, while the other index, as the pregnant weeks accumulate [10]. During the pregnant period, the concentrations of AFP and β-HCG as well as other material will be impacted by the age, weight, health, bad habits, race and so on. Therefore, the model of prenatal screening ought to be as follows: on the basis of the agreement of the pregnant women, relying on the technical situation of hospital the individualized prenatal screening and diagnosis strategy are supposed to be adopted. If necessary, it can combine with b-ultrasound examination in the early pregnant period.

3. Based on the calculation, the false positive rate got from pregnant week 16 to week 19 is obviously lower than the rates got from pregnant week 15 and the week 20($P<0.005$). So maybe the satisfied period to accept the prenatal screening if from pregnant week 16 to week 19.

4. The serological examination of pregnant women is a risk evaluation, which has its own limitations. Consequently, it is necessary to let the pregnant and her family knows the risk of the amnionic paracentesis as well as the uncertainty of the result [1], avoiding the negative impact on the screening.

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