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Original article

A study to assess the impact of maternal psycho-emotional health on childhood morbidity: a comparative study of ART and natural conception

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Abstract. The aim of this study was a longitudinal study to assess the impact of the psycho-emotional state of health of 252 mothers and the level of maternal care on the morbidity rate of acute respiratory infections in children born using assisted reproductive technologies (ART) and by natural conception. In addition, the effects of prematurity and low birth weight, Apgar scores, breastfeeding, and kindergarten attendance on the incidence of acute upper and lower respiratory tract infections in children in both groups were studied. We compared two comparable groups of healthy children aged 0 to 3 years and their mothers. The mothers' levels of anxiety and depression were determined, as well as the level of parental care for the child, and a personal interview was also conducted. The children were examined, as well as a history and analysis of medical records. Univariate and multivariate negative binomial regression analysis models were used for statistical analysis to assess the influence of predictors on child morbidity rates. The incidence of respiratory tract infections was significantly lower in the ART group. As a result of the study, we did not find a statistically significant effect of maternal anxiety and depression on the incidence of respiratory infections in their children in both groups. Our findings revealed that after the birth of a child, mothers in the ART group took better care of the long-awaited and often only child, which reduced the incidence of the disease in this group. (www.actabiomedica.it)

Key words: children, ART, depression, anxiety, respiratory diseases

Introduction

Since the birth of the first child using assisted reproductive technology (ART) in 1978, concerns have been raised regarding the health and development of children conceived through ART (1).

In Kazakhstan, these technologies were first applied in 1995. With the assistance of ART, more than 25,000 children were born, which has led to a growing interest in the impact of ART on offspring health in the country. However, this field of medicine has not been studied in the country before, and this is the first scientific work in Kazakhstan.

Since the first use of ART technology, a multitude studies have been conducted to investigate its impact on the subsequent physical and mental development of the child. Existing publications concerning the health status of children after ART have conflicting results. Short-term and long-term risks have been identified, confirming that major complications are associated with multiple pregnancies (1). Publications have revealed a significant increase in the incidence of cardiovascular, endocrine, neurological, and psychiatric diseases (2-7). There are few publications showing a high incidence of malformations among children conceived using ART (8,9).

The short-term outcomes for children born after ART are well-known from numerous publications, with higher rates of preterm birth and low birth weight in children (10). While the vast majority of low birth weight children have normal outcomes, as a group they generally have higher rates of subnormal growth, illness, and neurodevelopmental problems. These problems increase as the child's birth weight decreases. Adverse sociodemographic factors negatively affect developmental outcomes across the continuum of low birth weight and appear to have a far greater effect than most of the biological risk factors (11). The studies underscore the importance of a healthy social environment for children who are already at high risk for poor health outcomes due to low birth weight (12).

Caregiving behaviours are known to mediate between social, health and caregiver attributes and child survival, growth and development. They are a key determinant of the quality of the environment provided to children. It has been observed that caregivers of preterm babies interact with their infants differently than full-term infants. Goldberg's review (1978) review concluded that mothers of atypical babies, including premature and low birth weight infants, seem to work harder and carry more of the "interactive burden" than mothers of normal, healthy, full-term babies. They also found that maternal responsiveness had a modifying effect on infant irritability, thus diminishing the potential impact of the child's risk characteristic. In a study conducted in the Peruvian village, Gambirazo found that the best predictor of growth, after socioeconomic variables, was the love and affection that the caregiver gives to the child (14).

And here the psycho-emotional state of the caregiver, his or her ability to show care and love, comes to the fore.

Although interest in the psychological characteristics of women and couples with infertility problems is high, the impact of maternal psychological well-being on the psychosomatic status of the child when using ART has been understudied (15,16). Maternal mental health has been identified as a crucial factor influencing child development, affecting children's growth, cognitive development, and psychosocial well-being (17,18). The most common maternal mental disorder is depression, which affects one in seven women in the perinatal period (19,20).

There is strong evidence that maternal mental disorder has detrimental effects on the child's development (21). There is evidence that children of postpartum depressed mothers were more neurotic and exhibited more antisocial behavior than other children. Nineteen-month old toddlers whose mothers had postpartum depression showed significantly less affective sharing and less initial sociability with strangers, and were more likely to display marked distress during a brief separation from their mothers than toddlers of nondepressed mothers (22).

Additionally, available data suggests an association between maternal mental health problems and childhood respiratory illness. Several questions regarding this potential link remain unanswered. Specifically, previous studies have examined the association between caregiver mental health problems and asthma morbidity among pediatric patients with asthma (23). To our knowledge, the association between parental mental disorders and childhood respiratory illness has been little examined (24).

Previous investigations on this topic have focused on outcomes related to respiratory disease; however, there is no information on whether this effect is specific to respiratory illness or whether it may be more general, where parental psychopathology may be associated with a generally increased risk of any physical disorder in youth (25).

Some analyses showed that parental major depression was associated with a significantly increased likelihood of respiratory illness in subjects. The association persisted although it was somewhat attenuated after adjusting for age and sex. The association between parental major depression and respiratory illness in subjects remained statistically significant after adjusting for the effect of parental prenatal smoking, grandparental prenatal smoking, parental respiratory illness, and parental functional impairment (26).

The association between parental major depression and the the likelihood of respiratory illness in subjects appears to be somewhat specific to respiratory illness, inasmuch as parental major depression does not appear to similarly increase the likelihood of a wide range of other physical disorders in subjects (27).

It is known that children cared for in daycare exhibit a two to three times greater risk of acquiring infections, which impacts both on individual health and on the dissemination of diseases through the community, especially among other children in the family. The microorganisms responsible for these infections are the same ones that attack children cared for at home. Children who attend daycare, especially under 3 years of age, suffer from infectious episodes that are more severe and greater in number. Acute Upper Respiratory infections (J00-J06 of ICD-10), lower respiratory infections (J20-J22), and also influenza and pneumonia (J20-J22) are responsible for the majority of the episodes of infectious disease that occur at daycare, and are the most common cause of childhood disease in the general population (28).

However, there is no published information regarding the health status of children born after ART in terms of the incidence of their ARIs and what may affect their incidence. Respiratory diseases rank first among diseases in children and continue to be the leading cause of child mortality worldwide (29,30,31). The Global Burden of Disease Study 2015 estimates that ARIs cause more than 15% of under-five mortality. ARI remains the most frequent reason for hospitalization in children. In children under the age of 5, respiratory viruses are detected in up to 80% of ARI cases (32).

Furthermore, the infant's dependence on parents, its sensitivity to interpersonal contacts, and the fact that in the vast majority of cases the mother is the primary environment of the infant in the first months after birth, make the topic of postpartum depression extremely important (33). Maternal depression, anxiety and stress can become attempts in trying to show love and care for the child. Maternal attachment, sensitivity and parenting style are essential for healthy maturation of an infant's social, cognitive and behavioural skills, and depressed mothers often display less attachment, sensitivity and more harsh or disrupted parenting behaviours, which may contribute to reports of adverse child outcomes in children of depressed mothers (34).

Higher levels of parental warmth and lower levels of parental irritability and parent-to-parent conflict are consistently associated with more positive outcomes for children (35,36). The care that children receive has powerful effects on their survival, growth and development. Care consists of the behaviours and practices of caregivers who provide the food, health care, stimulation and emotional support necessary for children's healthy survival, growth and development…Not only the practices themselves, but also the way they are performed – in terms of affection and responsiveness to the child – are critical to a child's survival, growth and development (37). More controlling parents may be avoiding dangerous situations (e.g., installing baby gates to keep kids nearby and safe from hazards; selecting more structured child care environments for out of home care), and avoiding infections (providing clean and clutter free homes, less unsupervised contact with peers). Consistent with this interpretation, parental control was associated with fewer diagnosed respiratory illnesses (38). Both parental structure and support have been found to predict both better adherence to treatment regimens and glycemic control in children with diabetes (39). Injury rates have also been found to relate to parenting practices, including the use of structure and behavioural use of structure and behavioural control (40,41). In addition, there is some evidence of an association between parenting practices and children's health-related behaviours, such as nutrition, physical activity, and hygiene (42). These studies provide evidence that parenting behaviours influence various aspects of illness management and health-promoting behavior behaviours influence various aspects of illness management and health-promoting behaviour behaviours influence various aspects of illness management and health-promoting behaviour, which in turn affect children's health outcomes.

Thus, parental circumstances are crucial for children's growth and development (43,44), and since studies have shown that the maternal factor is the strongest predictor of negative outcomes for children (45-47), it is important to study the role of the mother. Based on our review, it can be seen that the proper care and love of mother, can significantly reduce the incidence of the most common childhood diseases caused by respiratory infections. At the same time, the mothers with reduced fertility, who have waited 12 months or more, experienced difficulties at the stage of conception and inadequate long and complex infertility treatment, are

often prone to anxiety and depression, which can affect the quality of their care. However, despite this need, the psycho-emotional state of the ART mother herself has been studied, a small amount of publications have been devoted to how the health and/or behaviour of the mother who has undergone ART is related to the health of her children (48-50). In our study, we wanted to find out whether the mental state of the mother who underwent the ART affects the incidence of acute respiratory infections in children and whether the incidence of these infections is associated with home care, as well as kindergarten attendance.

Patients and methods

Study population and baseline characteristics and follow-up procedures.

The study included two groups of mothers:

- the first group contained 120 mothers who underwent in vitro fertilization (IVF) and their 120 children. These were women suffering from primary or secondary infertility, who underwent in vitro fertilization to conceive and successfully gave birth to a conditionally healthy child.
- the second group consisted of 132 women who gave birth naturally and their 132 children.

For the validity of the study results and the comparability of the compared groups, multiple pregnancies were excluded from this study. According to the literature data it is known that, multiple pregnancies are an unfavorable factor and may cause impaired child health (1,3). We also excluded children with organic impairment of different organs, since also could affect the results of the study. The study included healthy and conditionally healthy children. Children were divided into two groups: group I - healthy children and group II - healthy children, but with functional and some morphological abnormalities, as well as reduced resistance to acute and chronic diseases, with the presence of risk factors, according to the classification of children's health, approved by Order of the Ministry of Health of the Republic of Kazakhstan dated March 16, 2011 No.145 "On approval of the Rules for conducting preventive medical examinations of target groups of the population."

The study's groups were formed through self-referral to social media ads (Instagram and parent chats). To comply with ethical standards, each mother signed an information consent form to conduct the study.

Children of both groups were examined. A detailed history was collected, as well as physical characteristics such as height and weight physical development assessment. Additionally, medical records (antenatal and perinatal anamnesis, anthropometric data at birth, frequency, and structure of their morbidity) were studied.

The following data were collected from mothers of both groups: level of anxiety and depression on the Hospital Anxiety and Depression Scale (HADS) scale, and level of care using the "Test to identify the measure of parental care for the child". Standardized psychodiagnostics in the form of an online conversation were also conducted. Psychological tests and a standardized diagnostic interview were performed by three certified psychologists.

The HADS scale was validated in Russian by "Scientific Center of Mental Health" of the Ministry of Education and Science of Russia, Moscow (51). HADS includes 2 subscales (HADS-A for anxiety assessment and HADS-D for depression assessment), each of which consists of 7 questions with 4 answer options, rated from 0 to 3 points. HADS has been widely used in practice around the world for many years, has been translated into 115 languages and is often used in international clinical trials. The assessment of internal consistency was carried out by calculating the Cronbach's alpha index. The Cronbach's alpha internal consistency coefficient was 0.90 for the entire scale, 0.84 for HADS-D and 0.86 for HADS-A. All values above 0.8, therefore, all questions of the scale and the corresponding subscales are consistent, homogeneous and evaluate the same parameters.

The "Test to identify the measure of parental care for the child" was developed by Russian psychologist Irina Markovskaya (52). The test includes 15 items that assess parental nurturance, responsiveness to child input, and nonrestrictiveness. This version of the test has been shown to have good concurrent and predictive

validity as a predictor of observed parent-child interactions and the quality of parent-child relationships. Reliability (interitem consistency) in the present sample was calculated for support, structure, and control (Cronbach's α = 0.78, 0.68, and 0.69, respectively) (36).

In addition, data were collected on the socioeconomic status of the family, the age of the mother at the birth of the child, marital status, and the state of maternal health.

As a dependent factor, we took the incidence of acute respiratory infections of the upper and lower respiratory tract in children in both IVF and natural conception groups, while the presence of anxiety and depression in the mother, the degree of family care, and low birth weight status in both groups, the Apgar score at 1 and 5 minutes of delivery, and body weight estimates during the follow-up and breastfeeding period up to 6 months and up to one year were considered as predictive variables.

The anxiety, depression status according to Stern, 2014 (53), breastfeeding status, premature status, and underweight status were recorded as binary data, while the Apgar scores were used as numerical data for analysis. Only care levels were used as ordinal data for analysis.

All data were analyzed using STATA 17.0. Descriptive statistics were used to summarize the characteristics of the study population. Means and standard deviations were calculated for continuous variables, and frequencies and percentages for categorical variables. The Two-Sample T-test, and Mann–Whitney U-test were used for comparing baseline continuous data according to their distribution. Fisher exact tests were used to compare proportions/categorical data. A paired T-test and Wilcoxon Signed Rank Test were applied to compare baseline and follow-up characteristics in progress. The significance level was set at 95% CI, $p < 0.05$ for all statistical tests.

We employed univariate and multivariate Negative binomial regression Analysis models to assess the impact of predictors on child illness rates between maternal mental health, family care and child illness rate, considering the count features of the morbidity rate (Mother factors model). As well as that the same models have been used, in the child predictive variables models (premature status, underweight status at birth, breastfeeding status, and Apgar scores). The Negative binomial regression were used due to the count nature of the dependent variables, and due to mean and variance difference and overdispersion casualties.

Model fit was evaluated by using Overdispersion assessment and goodness-of-fit tests (Akaike Information Criterion). The significance level was set at 95% CI, $p < 0.05$ for Coefficient estimates for all predictors.

Results

The baseline characteristics of both groups are represented in Table 1. The mean age of mothers in the IVF group was almost 5 years higher compared to the naturally conceived group, and the weight of newborns conceived naturally was higher 3378.4 (528.5); 3121.3 (679.4), respectively; p=0.0001). The frequency of cesarean section was significantly higher in the main group - 70% of cases, compared with the control group - 32.6% (p-0,01). The ratio of births to boys was similar in both groups, with the ratio of preterm to underweight babies being higher in the IVF group (p- 0.001). The mean Apgar score at 1 minute was 7.0250 (SD = 0.8837) for infants born with IVF and 7.1532 (SD = 0.9554) for babies conceived naturally, the Apgar score at 5 minutes was 8.0667 (SD = 0.7750) in newborn conceived by ART and 8.2252 (SD = 0.8055) in those conceived naturally. There were no significant differences in Apgar scores between the IVF group and naturally conceived babies at 1 or 5 minutes after delivery.

To determine socio-economic status, the availability of one's housing, the place of residence (urban or rural), the availability of living conditions, and the average level of family income have been considered. More than 85% of respondents in both groups lived in normal conditions. More than 90% of women were married in both groups. The socioeconomic status of families in both groups was similar (p-0.506).

In the IVF group alone, 80% of mothers were primiparous, while 34.8% of families in the control group had two or more children (p-0.001).

The development of children in both groups corresponded to their age. In both groups, the children were mainly looked after by mothers, and in both groups,

Table 1. Baseline characteristics

	IVF group (mean, SD)			Control (mean, SD)			P- value
Mother age (mean, SD)	34,342 (5,739)			29,038 (5,268)			0,0001
Number of children in the family	one child	96	80%	Two and more	46	34,8%	0, 001
Body mass at birth (grams)	3121,3 (679,4)			3378,4 (528,5)			0,001
Underweight and normal weight in newborns	Norm	95	79,17%	Norm	124	93,94%	0,001
	Under	25	20,83%	Under	8	6,06%	
	N=120			N=132			
Gender numbers/ratio of babies	Female	52	43,33%	Female	57	43,18%	1,000
	Male	68	56,67%	Male	75	56,82%	
	N=120			N=132			
Mode of delivery (cesarean/vaginal)	Cesarean Vaginal	84 36	70% 30%	Cesarean Vaginal	43 89	32,6% 67,4%	0,001
Premature babies	No	94	78,33%	No	129	97,73%	0,000
	Yes	26	21,67%	Yes	3	2,27%	
	N=120			N=132			
Apgar scale on the first min (mean, SD)	7,0250 (0,8837)			7,1532 (0,9554)			0,130
Apgar scale on 5th min (mean, SD)	8,0667 (0,7750)			8,2252 (0,8055)			0,066
Socio economic status	85% - normal; 15% - less than normal			89% - norm; 11%-less than normal			0,506

Abbreviations: IVF: in vitro fertilization; SD: standard deviation.

about 50% of mothers were on maternity leave, taking care of the child mainly, of which about 10% of mothers worked part-time from home. About 20% of mothers worked online. The rest of the moms worked full-time. The was difference among two groups in terms of percentage of children, who visited kindergarten (47.4%) in the control group, while only 24% in the main group (p- 0.001). Children were more trusted by grandmothers than by strangers. There were no cases of involving a nanny.

In the structure of morbidity in children with organic damage and mental disorders, the indicators were low no more than 5% and did not differ in both groups).

Thus, the groups of children were comparable in terms of gender, age, socioeconomic conditions, and level of development.

The results at the end of the follow-up for both groups are presented in Table 2. The frequency of breastfeeding up to 6 months of age was higher in the group with natural conception [families of 104 (78.79%) and 69 mothers (57.5%), respectively (p-value = 0.000)]. The same trend was observed for breastfeeding for 12 months (p=0.006). In terms of weight difference, newborns with natural conception were statistically heavier than newborns in the IVF group (p=0.000), these differences were quite significant (more than 1 kilogram in the mean difference (p=0.000)).

The rate of annual upper and lower respiratory tract diseases was higher in the group with natural conception [4,364 (2,853); 2,708 (2,402); p=0,000]. To explain these findings, we compared the incidence of respiratory morbidity between organized (kindergarten) and unorganized children in the control group (who did not attend kindergarten) (Table 4 - description of the results).

The anxiety level was not different between the mothers in the two groups, anxiety was detected in 21-22% of the tested mothers. The level of depression was high in both groups (57%; 61%, respectively). Overall, the level of care was higher in the IVF group (the mothers with hyperactive care number - 30 mothers in the IVF group versus 19 mothers in the natural conception group; p=0.037).

Negative binomial regression analysis models for maternal and child prognostic factors are presented in Table 3.

Table 2. Results at the end of the follow-up

Characteristics of the children at the end of the follow-up							
Breastfeeding until 6 months	No	51	42,5%	No	28	21,21%	0,000
	Yes	69	57,5%	Yes	104	78,79%	
	N=120			N=132			
Breastfeeding until 12 months	No	58	52,73%	No	46	34,85%	0,006
	Yes	52	47,27%	Yes	86	65,15%	
	N=110			N=132			
	Missing=10						
Age at the end of the follow-up (months, mean, SD)	16,70 (11,05)			17,43 (11,36)			0,407
Body mass at the end of the follow-up (grams)	10549 (3176)			11952 (2650)			0,000
The rate of annual illness (mean, SD)	2,708 (2,402)			4,364 (2,853)			0,000
Characteristics of mothers at the end of follow-up							
Anxiety test	5,381 (2,491)			5,045 (3,054)			0,340
Anxiety number	No	92	77,97%	No	104	78,79%	0,879
	yes	26	22,03%	Yes	28	21,21%	
	N=118			N=132			
	*=2						
Depression test	8,627 (3,186)			8,629 (2,956)			0,997
Depression number	No	50	42,37%	No	51	38,64%	0,606
	Yes	68	57,63%	Yes	81	61,36%	
	N=118			N=132			
	*=2						
The care level	36,254 (6,632)			35,242 (5,985)			0,209
The care level numbers	Less care	7	5,93	Less care	5	3,79	0,557
	Enough	81	68,64	Enough	108	81,82	0,018
	Hyper	30	25,42	Hyper	19	14,39	0,037
	N=118						
	*=2			N=132			

Abbreviation: SD: standard deviation.

In the IVF group – in univariate and multivariate models – where maternal factors modeling the presence of anxiety and depression and the level of care of the family during follow-up were taken into account, no statistically significant effect on the rate of child morbidity was shown. The regression coefficients for the presence of depression status, anxiety, and level of care in the univariate models were as follows: - anxiety = -0.0342532, p=0.866; depression = 0.1085068, p=0.524; Level of care = -0.1241131b p=0.482. The values did not differ much in the multivariate models, demonstrating statistical insignificance.

In models that took into account only infant factors with univariate and multivariate analyses, predictors such as preterm birth status, underweight (at birth and follow-up), and breastfeeding status at 6 and 12 months showed statistical insignificance (p≥0.05). Apgar scores as a predictor of morbidity in children, in univariate and multivariate models, also showed that they did not affect morbidity rate (Apgar at 1 minute: p=0.290; coef= -0.0976684 (-0.2784555, 0.0831186); Apgar at 5 minutes: p=0.268; coef=-0.1133637 (-0.3141347; 0.0874073)).

In the natural conception group, the presence of anxiety, depression, and care level demonstrated

Table 3. Negative binomial regression analysis models

Variable	Univariate analysis		Multivariate analysis	
	p-value	Coefficient (CI)	p-value	Coefficient (CI)
IVF group				
Maternal factors only model				
Anxiety presence (binary)	0.866	-0.0342532 (-0.4325903 0.364084)	0.939	-0.0156491 (-0.4181868 0.3868887)
Depression presence (binary)	0.524	0.1085068 (-0.2249697 0.4419834)	0.472	0.1227458 (-0.2119643 0.457456)
Care Level	0.482	-0.1241131 (-0.4700087 0.2217826)	0.451	-0.1352977 (-0.4873517 0.2167563)
Child factors model				
Premature status	0.265	0.2151011 (-0.1634602 0.5936624)	0.433	0.1941693 (-0.291473 0.6798116)
Underweight at birth	0.454	0.1482815 (-0.2397599 0.536323)	0.890	0.0367118 (-0.4853954 0.558819)
Underweight during follow-up	0.660	0.1747417 (-0.6026792 0.9521625)	0.759	-0.1247084 (-0.9229282 0.6735114)
Breastfeeding until 6 months	0.947	-0.0110081 (-0.3365735 0.3145573)	0.627	0.0901204 (-0.272882 0.4531227)
Breastfeeding until 12 months	0.987	0.0025151 (-0.3072547 0.312285)	0.702	0.0743605 (-0.3067549 0.4554758)
Apgar on 1st min	0.290	-0.0976684 (-0.2784555 0.0831186)	0.434	0.241479 (-0.3638953 0.8468533)
Apgar on 5th min	0.268	-0.1133637 (-0.3141347 0.0874073)	0.314	-0.349358 (-1.028848 0.3301324)
Natural conceive				
Maternal factors only model				
Anxiety presence (binary)	0.294	0.1380665 (-0.1199668 0.3960999)	0.332	0.1398624 (-0.1429557 0.4226806)
Depression presence (binary)	0.453	0.0854157 (-0.1377548 0.3085862)	0.578	0.0689054 (-0.1738051 0.3116158)
Care level	0.949	-0.0089441 (-0.2805809 0.2626926)	0.568	-0.0863515 (-0.3825854 0.2098824)
Child factors model				
Premature status	0.356	-0.3819346 (-1.192812 0.428943)	0.650	-0.2079705 (-1.104916 0.6889752)
Underweight at birth	0.045	-0.5336057 (-1.055704 -0.0115075)	0.192	-0.4351608 (-1.089402 0.2190804)
Underweight during follow-up	0.787	0.0704517 (-0.4398069 0.5807102)	0.695	0.1202415 (-0.4812165 0.7216995)
Breastfeeding until 6 months	0.713	-0.0493506 (-0.3118892 0.213188)	0.258	-0.1964669 (-0.536701 0.1437673)
Breastfeeding until 12 months	0.164	0.1627515 (-0.0664234 0.3919264)	0.135	0.2358511 (-0.0733931 0.5450954)
Apgar on 1st min	0.135	0.110464 (-0.0342157 0.2551436)	0.181	0.2058377 (-0.0956142 0.5072896)
Apgar on 5th min	0.333	0.0821568 (-0.0841812 0.2484949)	0.325	-0.1791276 (-0.5357219 0.1774668)

Abbreviation: CI: confidence intervals.

statistical insignificance in both univariate and multivariate analyses in maternal factors-only models (univariate models - anxiety p=0.294; depression p=0.453; care level p=0.949; multivariate models - anxiety p=0.332; depression p=0.578; care level p=0.568).

Models of childhood factors with univariate analyses in this group illustrate the very interesting results that low birth weight status was a significant predictor [p-value: 0.045; coefficient: -0.5336057; 95% confidence interval (CI): (-1.055704, -0.0115075)].

Table 4. Negative binomial regression analysis

Variable	Univariate analysis	
	p- value	Coefficient (CI)
IVF group		
Kindergarten visit status	0.001	0.6138978 (0.2553688 - 0.9724268)
Natural conceive		
Kindergarten visit status	0.130	0.2436079 (-0.0719898 - 0.5592055)

Abbreviation: CI: confidence intervals.

This ratio suggests that low birth weight is associated with a lower morbidity rate in this group (for every unit of increase in low birth weight, the logarithmic incidence of childhood morbidity decreases by about 0.5336). However, other predictors did not demonstrate any significance in both univariate and multivariate analyses.

Negative binomial regression analysis models for kindergarten attendance and morbidity rates are presented in Table 4.

During the follow-up period, additional data were collected. Our observations showed that the frequency of kindergarten attendance was different between groups. It should be noted that the frequency of visits was significantly higher in the control group (natural conception) compared to the IVF group (47.44% - 24%; p- 0.001 (Fischer's exact test)). For this reason, we also decided to perform a univariate negative binomial regression to test its effect on annual incidence.

In the IVF group, the coefficient in this analysis was 0.6138978 (Stand err: 0.1829263); P-value: 0.001, indicating a positive relationship between kindergarten attendance and the number of illnesses throughout the year, which increases by about 0.61. Thus, the model suggests that kindergarten attendance has a significant impact on morbidity.

In the natural conception group – Results show that kindergarten attendance has no statistically significant effect on incidence in this group (p= 0.130).

Discussion and conclusion

Thus, in our study, maternal factors such as depression and anxiety did not significantly affect the incidence of acute infections of the upper and lower respiratory tract in both study groups, although the incidence of depression was quite high, in more than half of the surveyed mothers in both groups. Despite the fact that the care level group was insignificant (p=0.482; p=0.451), it hurt the rate of respiratory morbidity in children, that is, it reduced its incidence. The results obtained from the effect of prematurity and low body weight in the two study groups allowed us to conclude that it is not the fact of being underweight, but the level of care or care of the child that plays a significant role in the incidence of respiratory morbidity. The lower the body weight, the more thorough the care and the fewer children suffer from infectious respiratory diseases. Thus, in the IVF group, despite of more significantly high ratio of premature and underweight infants (p- 0.001), the annual rate of respiratory diseases in children was significantly low (p=0,000) due to better care for the long-awaited baby and, usually single one in family. We need to take into account the age difference of more than 5 years, since, mothers in the IVF group were older and psychologically more prepared for being mother.

Kindergarten attendance was a significant risk factor and was proven in the IVF group by a significant positive relationship between kindergarten attendance and the rate of respiratory diseases during the year. In the natural conception group, no significant differences were obtained, although these children were significantly more likely to be organized, there is a tendency that perhaps with a larger sample, a significant difference can be confirmed. It is possible that in the natural conception group, the incidence of the disease was also influenced by the presence of other children in the family, and therefore the children who did not attend kindergarten were also more likely to get sick than those who did.

Additional studies with a larger sample of data are needed to confirm our findings, but within the framework of this study, we could assume that there might be a potential impact of the psycho-emotional state of the mother on the child's health. Infertility, unpleasant procedures, and fear of not having a child did not increase the incidence of depression and anxiety compared to naturally conceived mothers. Long wait and fear were eventually overshadowed by the joy of motherhood, the feeling of achieving the long-awaited goal,

and the sense of the value of life which made them more conscious and responsible for the upbringing of the child. This was noted by all mothers in our study in a face-to-face conversation. They valued their new status as mom much more, while mothers in the control group were not able to rate their motherhood as highly. Accordingly, these mothers provided more thorough care for the baby and created a more emotionally stable atmosphere, which acted as a measure to prevent infectious respiratory diseases and significantly reduced their frequency. During our study we did not face any limitations. Our research will be continued.

Abbreviations: ART: assisted reproductive technology; IVF: in vitro fertilization; ARI: acute respiratory infection; HADS: Hospital Anxiety and Depression Scale; SD: standard deviation; CI: confidence intervals.

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