

## FACTORS AFFECTING THE FORMATION OF UNDESCENDED TESTIS INCLUDING MATERNAL NUTRITIONAL HABITS

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### ABSTRACT

**Aim:** The reasons affecting the development of undescended testicles remain unclear. We aimed to investigate the factors affecting the formation of an undescended testis and especially the relationship between maternal nutrition and undescended testis formation.

**Methods:** This was a descriptive study. Mothers of term newborns with cryptorchidism and mothers who gave birth to a healthy male baby in the same period were visited in the obstetrics units of the hospital and were surveyed with questions a patient form and a diet form. Fifty-one types of foods that mothers consume during pregnancy were questioned.

**Results:** Cryptorchidism was more common in babies born to young mothers and/or fathers ( $p= 0.013$  and  $p= 0.029$  respectively). Cryptorchidism was more common in babies with low birth weight. A higher rate of cryptorchidism was observed in infants with high body temperature measurements ( $p<0.001$ ). The rate of giving birth to babies with cryptorchidism was lower in mothers who consumed more dried foods ( $p=0.001$ ).

**Conclusion:** Increased temperature of the infants was an important risk for cryptorchidism. The reasons that will cause temperature changes in the infants should be carefully considered during pregnancy and the necessary interventions should be made. Consumption of dried foods and higher child birth weight may be protective against cryptorchidism. These findings suggest that high nutritional and caloric values in dried foods may contribute positively to the development of the intrauterine fetus and show that it can be a useful tool in preventing low birth weight, which is one of the risk factors. Maternal nutrition may be one of the effective causes of cryptorchidism development in infants.

**Keywords:** Dried food, low birth weight, parental age, temperature, undescended testis

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**Received:** December 23, 2024; **Accepted:** December 31, 2024; **Published Online:** December 31, 2024

**Cite this article as:** Yilmaz, A., Demirci, H., Sancar, S. & Satir, A. (2024). Factors Affecting the Formation of Undescended Testis Including Maternal Nutritional Habits. European Journal of Human Health 4(4),108-118.



## INTRODUCTION

Cryptorchidism is a common childhood disease. While the condition is seen at a rate of 1.0-4.6% in term babies, it can be observed in a wide range of rates such as 1.1-45% in preterm babies. After spontaneous descent in the first months of life, the incidence of undescended testes in one-year-old term babies regresses to 1% [1].

The key factors involved in the formation of cryptorchidism still remain elusive. It is assumed that the descent of the testicles occurs in two phases controlled by hormones. However, the reasons and mechanisms in the formation of the cryptorchidism are still not clearly explained [2].

Today, the causes and risk factors contributing to the development of cryptorchidism and the effects of maternal nutrition, lifestyle, and occupational and environmental exposures on this development are discussed as important issues in research [3-5]. In this study, we aimed to investigate the factors affecting the formation of cryptorchidism and especially the relationship between maternal nutrition and cryptorchidism formation.

## Methods

### Study Design and Study Population

The study protocol was approved by the University of Health Sciences Bursa Yuksek Ihtisas Training and Research Hospital's Clinical Research Ethics Committee with approval number 2011-KAEK-25 2018/07-14. The study was conducted in Bursa between November 2018 and June 2020. Newborn babies were examined in the

obstetrics clinic between the study periods. Newborns with cryptorchidism and their mothers were included in the study as the case group. The healthy infants who were born just after the infant with cryptorchidism and their mothers were included in the control group.

### Data collection and assessment

This was a descriptive study. A face-to-face survey technique was used. Consent forms were obtained from all volunteers for participation in the study. Mothers of newborns were visited in the obstetrics units of Bursa Yuksek Ihtisas Training and Research Hospital and were surveyed with questions using a patient form and maternal nutritional habits form.

The patient form, in which the demographic and clinical characteristics of the mothers and babies in the groups were questioned, and the maternal nutritional habits form, which questioned the diet of the mothers, were filled in by the researcher through face-to-face interviews and recorded. A cryptorchidism examination was also conducted by a pediatric surgeon. The mother's age, height, weight, number of live births, weight gained during pregnancy, history of birth with the anomaly, father's age, birth week of the baby, APGAR score, birth weight, and the presence of a concomitant external genital anomaly were questioned. Body temperatures of mothers and children were measured at the clinics where the babies were examined for cryptorchidism in the 24 hours after the birth. The armpit method was

used to measure the temperature of the babies and the mothers.

The maternal nutritional habits form is based on the principle that mothers indicate their food or beverage consumption at every meal, every day, 3-5 times a week, once every 15 days, and once in a month. The forms were filled in by the researcher by interviewing the mothers.

### Statistical analysis

The data obtained were analyzed using the SPSS Statistical Package® 21.0 package program. With all statistical analyses,  $p < 0.05$  was accepted as the level of significance, and the relationships were evaluated within the 95% confidence interval. The relationship between categorical dependent and independent variables was evaluated with Fisher Freeman-Halton tests and the relationship between numerically dependent and categorical independent variables was evaluated with Mann-Whitney U tests.

### Results

During the study period, 4994 newborn babies were examined and 51 of them were found to have cryptorchidism. One hundred and two mothers participated in the study, including mothers of infants with cryptorchidism ( $n=51$ ) and the control group ( $n=51$ ). The mean maternal age was 28.02 ( $\pm 4.93$ ) in the patient group and 30.37 ( $\pm 5.11$ ) in the controls; the mean age of the father was found to be 32.18 ( $\pm 5.10$ ) in the patient group and 34.10 ( $\pm 5.91$ ) in the control group. Cryptorchidism was more common in babies born

to young mothers and/or fathers ( $p = 0.013$  and  $p = 0.029$  respectively). There was no difference between the groups in terms of the mother's height, weight, and the father's age. The mean temperature of the mother was 36.78 ( $\pm 0.92$ ) °C in the patient group and 36.68 ( $\pm 0.31$ ) °C in the control group ( $p = 0.059$ ). The mean temperature of the infants was 36.94 ( $\pm 0.27$ ) °C in the patient group and 36.55 ( $\pm 0.40$ ) °C in the control group ( $p < 0.001$ ). A relationship was found between the cryptorchidism and the measured temperature of the infants (Table 1).

The mean birth weight was 2852.20 ( $\pm 901.30$ ) grams in the patient group and 3199.53 ( $\pm 732.99$ ) grams in the controls ( $p = 0.035$ ). Accordingly, the cryptorchidism was more common in babies with low birth weight. There was no difference between the groups in terms of APGAR score, week of birth, and accompanying external genital anomalies (Table 1).

The relationship between maternal dietary habits and cryptorchidism is shown in Table 2. Accordingly, the rate of giving birth to babies with cryptorchidism was lower in mothers who consumed more dried foods ( $p = 0.001$ ).

According to Multivariate Binary Logistic Regression Analysis, it was found that an increase in temperature of the infants increased the risk of cryptorchidism by 57.40 times ( $p < 0.001$ ), and an increase in maternal dried food consumption (OR=0.749,  $p = 0.037$ ) and child birthweight (OR=0.999,  $p = 0.008$ ) values decreased the risk of cryptorchidism (Table 3).

**Table1. General characteristics of the participants (babies and mothers)**

	Control Group (mean±SD)	Case Group (mean±SD)	p-value
Mother age (years)	30.37(±5.11)	28.02(±4.93)	0.013
Mother height (cm)	159.94(±5.45)	161.61(±6.16)	0.148
Mother weight (kg)	75.28(±11.17)	76.63(±15.83)	0.944
Weight gained of mothers during pregnancy (kg)	11.24(±5.21)	11.61(±6.35)	0.760
Mother Body Mass Index (kg/m <sup>2</sup> )	26.28(±4,929)	24.89(±5.59)	0.081
Number of live births	2.20(±1.11)	2.08(±0.89)	0.828
Father's age (years)	34.10(±5.91)	32.18(±5.10)	0.029
Temperature of the mothers (°C)	36.68(±0.31)	36.78(±0.92)	0.059
Temperature of the infants (°C)	36.55(±0.40)	36.94(±0.27)	<0.001
Apgar 1 <sup>st</sup> minute	9.90(±0.30)	9.66(±0.92)	0.302
Apgar 5 <sup>th</sup> minute	8.82(±0.63)	8.72(±0.73)	0.265
Birth weight of the baby (kg)	3199.53(±732.99)	2852.20(±901.30)	0.035
Birth week of the baby	37.47(±2.81)	36.67(±3.34)	0.245

**Table 2: Food group consumption of mothers of infants with and without cryptorchidism**

Food	Control Group (mean±SD)	Case Group (mean±SD)	p-value
Milk	3.35±2.43	2.92±2.19	0.309
Yoghurt	4.86±1.65	4.90±1.46	0.890
Cheese	5.37±1.57	5.49±1.17	0.757
Meat	2.90±1.71	2.43±1.76	0.187
Chicken	2.43±1.65	2.43±1.57	0.782
Offal	0.25±0.69	0.37±1.06	0.761
Prepared meat products	0.92±1.25	1.06±1.42	0.741
Homemade meat and meat products	0.33±0.93	0.72±1.64	0.322

Egg	4.96±1.55	4.88±1.73	0.957
Legumes (beans, chickpeas, lentils, etc.)	3.02±1.19	2.84±1.16	0.378
Hazel nut	3.98±1.97	3.49±2.00	0.219
Green leafy vegetables	4.29±1.75	4.22±1.54	0.651
Potatoes	4.04±1.23	3.51±1.33	0.071
Other fresh vegetables	4.29±1.59	3.94±1.39	0.153
Dried fruits and vegetables (Figs, apricots, grapes)	2.57±2.17	1.20±1.59	0.001
White bread	5.33±1.63	5.35±1.49	0.992
Whole grain	1.24±2.23	1.51±2.27	0.370
Rice	4.12±1.24	3.73±0.94	0.075
Tarhana (traditional soap)	1.48±1.72	2.06±2.04	0.261
Biscuits	2.53±2.18	3.06±2.01	0.192
Food for breakfast	0.49±1.30	0.80±1.59	0.174
Simit	1.98±1.44	1.51±1.57	0.055
Prepared foods	1.38±1.81	1.43±1.71	0.572
Carbonated drinks	0.98±1.57	0.82±1.03	0.678
Mineral water	2.16±2.44	2.27±2.27	0.614
Coffee	2.80±2.51	2.24±2.21	0.220
Tea	4.69±2.34	4.37±2.29	0.337
Herbal tea	0.75±1.48	0.63±1.41	0.567
Alcoholic beverages	0.12±0.84	0.00±0.00	0.317
Olive oil	2.80±2.66	3.25±2.55	0.269
Hazel nut oil	0.08±0.44	0.00±0.00	0.155
Sunflower oil	4.90±1.94	5.08±1.87	0.433
Corn oil	0.20±1.00	0.32±1.22	0.244
Soy Oil	0.00±0.00	0.02±0.14	0.317
Canola Oil	0.12±0.84	0.02±0.14	0.989
Hard margarine	0.86±1.76	1.31±1.96	0.147

Soft margarine	0.86±1.78	1.06±1.89	0.496
Butter	3.65±2.26	3.49±2.57	0.919
Lard	0.37±1.08	0.33±1.13	0.432
Sugar, honey, jam, molasses	3.63±2.39	3.41±2.39	0.598
Confectionery, Turkish delight, chocolate	2.65±2.05	2.76±2.37	0.881
Packaged soup	0.60±1.26	0.71±1.59	0.871
Convenience food	0.12±0.52	0.53±1.25	0.035
Pita, lahmacun (Turkish pizza), pizza, etc.	0.82±0.93	1.12±1.03	0.122
Doner, kebab, etc. (traditional meat)	0.92±1.00	0.94±1.05	0.977
Hamburger, fried chicken pieces	0.39±0.96	0.35±0.80	0.602
Chips	0.78±1.38	1.20±1.60	0.158
Frozen food	0.37±1.13	0.41±0.88	0.263
Pastry dessert	1.92±1.72	1.78±1.64	0.661
Milk dessert, ice cream	2.16±1.97	2.22±1.78	0.751

**Table 3 Factors that increase the risk of cryptorchidism**

	B	se	Wald	df	p	OR	95% CI	
							Lower	Upper
Age	-.177	.098	3.236	1	0.072	0.838	.691	1.016
Father age	.083	.087	.906	1	0.341	1.086	.916	1.287
Temperature of the infants	4.050	1.002	16.347	1	<0.001	57.403	8.059	408.885
Child birth weight	-.001	.000	6.947	1	0.008	0.999	.998	1.000
Dried food	-.289	.138	4.355	1	0.037	0.749	.571	.983
Convenience food	.462	.366	1.590	1	0.207	1.586	.774	3.251

NR2=0.41, X2=53.30, p<0.001, Multivariate Binary Logistic Regression Analysis.

## Discussion

In the present study, younger mothers, younger fathers, and low birth weight were found to be associated with cryptorchidism. Increased temperature of the infants was a risk for cryptorchidism. Consumption of dried foods and higher child birth weight decreased the risk of cryptorchidism.

A higher rate of cryptorchidism cases was seen in the children of younger mothers. In this regard, we encounter studies that present different results in the literature. For example, Jones [6] and McGlynn [7] observed that young age (<20 years) has a protective effect against the development of cryptorchidism. Wagner-Mahler et al., on the other hand, could not detect any relationship between maternal age and cryptorchidism in newborn children [8]. Considering these findings, it is difficult to come to a clear conclusion on the relationship between maternal age and the development of cryptorchidism, but considering the whole of the studies, they provide more valuable information on finding an ideal age range where the development of cryptorchidism is less. Being young regarding maternal age can affect intrauterine fetal development in various ways such as at the anatomical, hormonal, environmental, psychological, socio-economic, and educational levels.

Paternal effects in terms of reproductive health receive a lot of attention. In recent years, extensive studies have been conducted on the effect of advanced maternal and paternal age on

the frequency of genetic chromosomal anomalies [9-11]. Various researchers have attempted to find a relationship between increasing paternal age and semen quality, but they could not obtain results showing a linear relationship with increasing age [12-15]. Studies generally establish a strong relationship between advanced paternal age and chromosomal anomalies and the syndromes caused by these anomalies. Stillbirth rates seem to be associated with advanced paternal age. For example, in a study conducted in 2017, stillbirth rates were found to be highest for fathers with older age, while it was observed to be higher in fathers with younger age [16]. In the present study, we observed higher rates of cryptorchidism in children of younger fathers. When this finding is evaluated together with other studies, a relationship can be established between paternal cigarette consumption at young ages and cryptorchidism development [17-19]. Cigarette consumption levels in young individuals may be under-reported for social reasons. The lack of a clear consensus on the definition of advanced paternal age also makes it difficult to draw clear conclusions.

As is known, the testicles are in a lower temperature environment than the intra-abdominal organs due to their scrotal location and provide an ideal environment for sperm development. In our study, we observed a higher rate of cryptorchidism in children with high body temperature measurements. There can be many reasons such as immunological causes, infectious diseases, and other febrile conditions may cause this situation.

However, since the number of cases was low in the present study, the results must be interpreted with caution.

Many researchers blame some of the food products consumed and the potentially dangerous chemicals in these products for many of the diseases seen frequently today [20-22]. Giordano et al.[23] have observed that the development of cryptorchidism was higher in the children of mothers with high consumption of smoked food products, and suggested that potentially toxic products to be found in foods may cause various urogenital anomalies. Brantsæter et al. [16] have conducted some studies to examine the role of organic food consumption during pregnancy in the development of hypospadias and cryptorchidism in children in a study conducted in Norway in 2015 with the participation of 35 thousand mothers. According to the results of this study, it was observed that the risk of cryptorchidism development decreased in the group that consumed vegetables, milk, and dairy products among the questioned organic foods, but it could not find a strong relationship in terms of organic food consumption and the development of cryptorchidism. We observed significant findings in terms of the low risk of development of cryptorchidism with consumption of dried food (apricot, fig, grape). Basically, this finding makes us think that high nutritional and caloric values in dried foods may make a positive contribution to intrauterine fetal development and shows that it can be a useful tool in preventing low birth weight, which is one of the most important risk

factors. However, it needs to be explained how the low liquid ratio in the nutritional character contributes to the prevention of cryptorchidism.

Cryptorchidism has been strongly associated with low birth weight, gestational age, and size for gestational age [24]. One of the most prominent risk factors associated with the development of cryptorchidism is low birth weight, which is also considered an important risk factor in many other congenital anomalies [25-28]. In our study, we observed a higher rate of cryptorchidism in infants with low birth weight, consistent with other studies in the literature.

## Conclusions

Increased temperature of the infants was an important risk for cryptorchidism. The reasons that will cause temperature changes in the infants should be carefully considered during pregnancy and the necessary interventions should be made. Consumption of dried foods and higher child birth weight may be protective against cryptorchidism. This suggests that high nutritional and caloric values in dried foods may contribute positively to the development of the intrauterine fetus and shows that it can be a useful tool in preventing low birth weight, which is one of the risk factors. Maternal nutrition may be one of the effective causes of cryptorchidism development in infants.

**Competing interests:** There are no conflicts of interest

**Funding:** Not Applicable



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