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RESEARCH ARTICLE

Investigating Factors Related to the Occurrence of Premature Infants in the South of Iran: A Population-based Study

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Abstract:

Background:

Prematurity has been recognized worldwide as the leading cause of death in infants under 4 weeks of age for at least a decade. This study aimed to investigate the factors related to the occurrence of premature infants in the south of Iran in 2020.

Methods:

In this cross-sectional study, the reporting of premature birth infants was done from the national system of the Ministry of Health (Iman). In the next step, according to the checklist made by the researcher, the information was extracted from the SIB system and completed by a survey of the mothers. Premature infants whose prematurity disorder occurred from March 21, 2019, to March 19, 2020, formed the study cohort. Analyses of the data used SPSS v 20 software, and the statistical significance level was set at <0.05.

Results:

In this study, 554 premature infants were examined, and about 55% of them were boys. The residence of the parent's premature infants was the village (58.5%). The more common factors seen with PTBs were an unwanted pregnancy, hemoglobin less than 11, Body Mass Index (BMI) more than 30, pre-eclampsia, gestational diabetes, opium use in family members, history of cesarean section in previous pregnancies, low family monthly income, low education, and nonprofessional occupations of the mother and father.

Conclusion:

Spontaneous premature infants were common in socially vulnerable groups, such as rural residents or people with low education and a poor economic situation. It is emphasized that the reduction of social and health inequalities will likely reduce premature birth rates.

Keywords: Risk factors, Premature, Infants, Population, Health, Prematurity disorder.

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1. INTRODUCTION

The global burden of preterm birth (PTB) includes the morbidity and mortality of infants born before 37 weeks of gestation [1]. Prematurity has been the leading cause of death in infants worldwide for at least a decade, but it has now also become the leading cause of death in children under five years of age. Worldwide, 15 million premature infants are born each year, which is estimated to account for about 11% of all births. Preterm birth appears to be increasing in most countries [1, 2]. Premature infants (28 weeks pregnant) account for only about 0.7 percent of births in the United States and an even smaller proportion in other developed and wealthy countries. However, these births comprise a disproportionate number of children with cerebral palsy, intellectual disability, autism spectrum disorder, attention deficit hyperactivity disorder, and epilepsy. Among people born prematurely, there is an increased risk of more neurodevelopmental disorders. Early life factors that contribute to this risk include perinatal brain injury, broncho-

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pulmonary dysplasia, and neonatal systemic inflammation. It seems that prenatal factors, especially the socio-economic status of the family, also play a role in creating risk. For most adverse outcomes, the risk is greater in male births [2]. A prior study noted that black women (who may have greater socioeconomic disparities than white women in the US) have a higher PTB rate (14% compared to 9%) [3].

Psychosocial factors, such as depression and other social determinants of health (SDH) which are associated with shorter gestational age (*e.g.*, not receiving health services), can increase the risk of PTB. A large number of premature children have short-term and long-term cognitive, social-emotional, mental health, behavioral and supervisory problems up to school age and beyond [4]. In general, several multifaceted factors that can be classified as biological-medical risks, psychosocial risks, and SDH can be considered the causes of prematurity [2, 5]. Biomedical risks of PTB include high blood pressure, being underweight and having other medical disorders, multiple pregnancies, inflammation and infections, uterine abnormalities, and a variety of genetic disorders. In addition to psycho-social risk factors, such as depression and anxiety, stress, traumatic events, lack of social support and some individual/household factors, such as low levels of education, housing insecurity, and transportation limitations, are associated with PTB [5, 6]. Premature infants can also be a major source of stress in a parent's life. After birth, parents (of a PTB) may find themselves in an unfamiliar and highly technological environment that can be overwhelming as they adjust to their new role as parents of a preterm infant. Uncertainty related to infant health risks and complex parenting needs due to the prematurity of the baby leaves the parents under significant psychological pressure [4]. Therefore, the prevention of prematurity of infants is considered a public health priority to reduce the mortality rate of infants and children related to this disease, but unfortunately, relatively little progress has been made in preventing PTBs. One of the biggest challenges in studying this disease is that PTB is a complex condition that results from multiple etiological pathways [7].

PTB is a complex trait determined by multiple environmental and genetic factors. There is a critical need to move beyond traditional approaches to dealing with PTB [3]. Despite the reported association between PTB and a wide range of sociodemographic, medical, obstetric, fetal, and environmental factors, approximately two-thirds of PTBs occur without an obvious risk factor [8]. Therefore, more research is needed to understand the multiple factors associated with prematurity and to identify effective interventions to prevent this problem [6, 8].

To add to the body of literature identifying factors associated with PTB internationally and focusing on the lower socioeconomic Kerman province *versus* other parts of Iran, the researchers investigated PTB cases in the rural south of Iran.

2. METHODS

In this cross-sectional study, first, the national code of mothers of premature infants was extracted by reporting from the national system of the Ministry of Health (Iman) (the Iman system is one of the most comprehensive systems of the Ministry of Health, which registers their information at the same time as the baby is born in the hospital), in the next step, we identified 554 premature infants by entering the national code of mothers (only Iranian mothers) in the SIB system, additional information was collected from the SIB system and a follow-up survey of mothers using a checklist made by the research team which was derived from various scientific sources and review articles and approval by PTB content experts. Some information was obtained from the electronic file of maternal care in the SIB system. Premature infants whose prematurity disorder occurred from April 1, 2019, to the end of March 2020 were recorded in the SIB system and followed up as above. To complete the predetermined data checklist, demographic information (such as baby's sex, mother's age, mother's education, father's education, *etc.*, information related to the mother's pregnancy history (such as the history of cesarean section in previous pregnancies, history of premature infants, history of stillbirth, history of abortion, a history of using addictive substances) and information related to recent pregnancies (such as the number of the birth, pregnancy order, polyhydramnios, pre-eclampsia, Infectious disease, concurrent infectious disease, use of birth control methods, placenta previa and gestational diabetes) were used.

During the phone call with the mother, the survey included information, such as the history of using family planning techniques, domestic violence, employment, and educational information regarding the baby's father, the family's monthly income and the source of drinking water that was not available in the Iman system data. The data collection tool also included the demographic characteristics of the baby, the baby's mother and father, the place of residence, and the risk factors related to the mother and the baby that could possibly be related to the occurrence of prematurity.

Data analysis was done using SPSS version 20 software. Descriptive statistics (number, percentage, mean and standard deviation) and subsequent analysis of demographic variables were used in a one-way analysis of variance, chi-square, t-test, and Spearman's correlation. The statistical significance level was set at a *p-value* <0.05.

3. RESULTS

In this study, 554 premature infants were examined, and about 55% of them were male. About 80% of the mothers of premature infants were between 18 and 35 years old. In terms of education, most mothers and fathers had primary education (13.7% and 20%, respectively), most of the mothers were housewives (87.9%), and most of the fathers were farmers/ranchers (37%). The residence of the parents of most premature infants was the village (58.5%) (Table **1**).

The most common factor in PTBs was the history of cesarean section in previous pregnancies (49.8 percent), followed by the history of miscarriage (21.3 percent), the history of premature infants (9.4 percent), and the history of stillbirth (3.8 percent) and a history of using addictive substances (1.6 percent) (Table **2**).

Table 1. Status of demographic variables of study participants.

Variable		Number (Percent)	Variable		Number (Percent)
Gender of the baby	Girl	247 (44.6)	Mother's job	Employee	32(5.8)
	Boy	307 (55.4)		Housewife	487 (87.9)
Mother's age in the recent pregnancy	Less than 18 years	12(2.2)		Farmer/rancher	9(6.1)
	18 to 35	437 (78.9)		Other	26(4.7)
	More than 35	105(19)	Father's job	Employee	65 (11.7)
Mother's education	Illiterate	34(6.1)		Farmer/rancher	205(37)
	Diploma and less	397 (71.7)		Other	271 (48.9)
	University	123(22.2)		Unemployed	13(2.3)
Father's education	Illiterate	47(8.5)	Monthly family income	Less than 5 million	102 (18.4)
	Diploma and less	402 (72.6)		5 to 10 million	219 (39.5)
	University	105(19)		More than 10 million	233(42.1)
Address	City	230 (41.5)	Type of residential house	Personal	422 (76.2)
				Rental	132 (23.8)
	Village	324 (58.5)	Drinking water source	Piping network	512 (92.4)
				Other	42(7.6)

Table 2. Frequency of historical factors in the PTB cohort.

Variable	Number (Percentage)
Cesarean sections in previous pregnancies	276 (49.8)
Prior premature infants	52 (9.4)
Prior stillbirth	21 (3.8)
Prior abortion/miscarriage	118 (21.3)
Use of addictive substances by the mother	9 (1.6)

Table 3. Frequency of common pregnancy-related health factors and premature births in the context of recent pregnancy.

Variable		Number (Percent)	Variable		Number (Percent)
Number of the births	Single	465 (83.9)	Distance to previous pregnancy	No history of pregnancy	141 (25.5)
	2≤	89 (16.1)		Less than a year	22 (4)
Pregnancy order	First	148 (26.7)		One to two years	72 (13)
	2 – 5	386 (69.7)		More than two years	319 (57.6)
	6 ≤	20 (3.6)	Choice in pregnancy	with authority	456 (82.3)
Polyhydramnios	Yes	23(4.2)		Unwanted	98 (17.7)
	No	531 (95.8)	Use of addictive substances by the mother	Yes	6 (1.1)
Pre-eclampsia	Yes	77 (13.9)		No	548 (98.9)
	No	477 (86.1)	Type of addictive substance used	None	548 (98.9)
Infectious disease	Yes	59 (10.6)		Drugs	5 (0.9)
	No	495 (89.4)		Tranquilizers	1 (0.2)
Type of infectious disease	None	492 (88.8)	Addictive drug use in family members	None	435 (78.3)
	Urogenital	47 (8.5)		Opium	60 (10.8)
	Sexually transmitted infection	7 (1.3)		Cigarettes	35 (6.3)
	Viral disease	4 (0.7)		Hookah smoking	20 (3.6)
	Other infections	4 (0.7)		Other	5 (0.9)
Use of birth control methods	Yes	29 (5.2)	Rupture of water sac during pregnancy	Yes	59 (10.6)
	No	525 (94.8)		No	495 (89.4)
Placenta previa	Yes	15 (2.7)	Placental Abruption	Yes	7 (1.3)
	No	539 (97.3)		No	547 (98.7)
Gestational Diabetes	Yes	66 (11.9)	Psychopathy	Yes	8 (1.8)
	No	488 (88.1)		No	546 (98.6)

(Table 3) contd.....

Variable		Number (Percent)	Variable		Number (Percent)
Domestic violence	Yes	9 (6.1)	Stomach kick	Yes	5 (0.9)
	No	545 (98.4)		No	549 (99.1)
Presence of uterine disorders	Yes	5 (0.9)	Cervical insufficiency	Yes	10 (1.8)
	No	549 (99.1)		No	544 (98.2)
Contact with chemical toxins	Yes	5 (0.9)	Having underlying diseases	No	426 (76.9)
	No	549 (99.1)		Cardiovascular	5 (0.9)
Body mass index	≤18	44 (7.9)		Diabetes	29 (5.2)
	18 – 25	274 (49.5)		Psychological	3 (0.5)
	25 to 30	152 (27.4)		Kidney	10 (1.8)
	More than 30	84 (15.2)		Hepatic	8 (1.4)
Having pyelonephritis	Yes	13 (2.3)		Bloody	14 (2.5)
	No	541 (97.7)		Immunodeficiency	1 (0.2)
Periodontal diseases	Yes	34 (6.1)		Other	58 (2.5)
	No	520 (93.9)			
Maternal hemoglobin in the first 3 months of pregnancy	≤11	89 (16.1)	Maternal hemoglobin in the second 3 months of pregnancy	<10.5	89 (16.1)
	11≤	465 (83.9)		10.5<	465 (83.9)

Table 4. Statistical relationship between the number of potential risk factors and the risk of PTB.

Variable		Specific Potential Risk Factors and their Association with the Number of other Potential Risk Factors in this Cohort of PTBs						*p-value*
		No. Risk Factors		1 and 2 Risk Factors		3 and 4 Risk Factors		
		Number	Percent	Number	Percent	Number	Percent	
Gender of the baby	Girl	109	49.8	129	41.1	9	42.9	0.137
	Boy	110	50.2	185	58.9	12	57.1	
Mother's age in the recent pregnancy	≤18	8	3.7	4	1.3	0	0	0.004
	18 -35	183	83.6	241	76.8	13	61.9	
	35≤	28	12.8	69	22	8	38.1	
Mother's education	Illiterate	17	7.8	16	5.1	1	4.8	0.710
	Diploma and less	155	70.8	228	72.6	14	66.7	
	University	47	21.5	70	22.3	6	28.6	
Father's education	Illiterate	22	10	24	7.6	1	4.8	0.433
	Diploma and less	150	68.5	237	75.5	15	71.4	
	University	47	21.5	53	16.9	5	23.8	
Mother's job	Employee	11	5	19	6.1	2	9.5	0.222
	Housewife	201	91.8	268	85.4	18	85.7	
	Farmer/rancher	1	0.5	8	2.5	0	0	
	Other	6	2.7	19	6.1	1	4.8	
Father's job	Employee	24	11	39	12.4	2	9.5	0.669
	Farmer/rancher	83	37.9	115	36.6	7	33.3	
	Other	110	50.2	150	47.8	11	52.4	
	Unemployed	2	0.9	10	3.2	1	4.8	
Monthly income	<5 million	37	16.9	58	18.5	7	33.3	0.356
	5 - 10 million	91	41.6	123	39.2	5	23.8	
	10< million	91	41.6	133	42.4	9	42.9	
Type of residential house	Personal	160	73.1	243	77.4	19	90.5	0.150
	Rental	59	26.9	71	22.6	2	9.5	
Drinking water source	Piping network	201	91.8	292	93	19	90.5	0.823
	Other	18	8.2	22	7	2	9.5	
Address	City	89	40.6	134	42.7	7	33.3	0.663
	Village	130	59.4	180	57.3	14	66.7	

Table 5. Association of specific risk factors with a number of other PTB risk factors.

Variables		Frequency of PTB as a Function of the Number of Potential Risk Factors Associated with Recent Pregnancies				*p-value*
		Up to 8 Risk Factors		More than 8 Risk Factors		
		Number	Percent	Number	Percent	
Gender of the baby	Girl	240	44.7	7	42.2	0.77
	Boy	297	55.3	10	58.8	
Mother's age in the recent pregnancy	≤18	12	2.2	0	0	0.74
	18 -35	424	79	13	76.5	
	35≤	101	18.8	4	26.5	
Mother's education	Illiterate	30	5.6	4	23.5	0.00
	Diploma and less	388	72.3	9	52.9	
	University	119	22.2	4	23.5	
Father's education	Illiterate	44	8.2	3	17.6	0.03
	Diploma and less	392	73	10	58.8	
	University	101	18.8	4	23.5	
Mother's job	Employee	32	6	0	0	0.49
	Housewife	470	87.5	17	100	
	Farmer/rancher	9	17	0	0	
	Other	26	4.8	0	0	
Father's job	Employee	65	12.1	0	0	0.34
	Farmer/rancher	199	37.1	6	35.3	
	Other	261	48.6	10	58.8	
	Unemployed	12	2.2	1	5.9	
Monthly income	Less than 5 million	95	17.7	7	41.2	0.04
	5 to 10 million	213	39.7	6	35.3	
	More than 10 million	229	42.6	4	23.5	
Type of residential house	Personal	410	76.4	12	70.6	0.58
	Rental	127	23.6	5	29.4	
Drinking water source	Piping network	496	92.4	16	94.1	0.78
	Other	41	7.6	1	5.9	
Address	City	221	41.2	9	52.9	0.33
	Village	316	58.8	8	47.1	

The frequency of maternal pregnancy factors (including complications) is shown in Table **3**. The most common factor was unwanted pregnancy (17.7%), hemoglobin less than 11 (16.1%), body mass index (BMI) greater than 30 (15.2 percent), pre-eclampsia (13.9%), gestational diabetes (11.9%), opium use in family members (10.8%), and water sac rupture (10.6%).

There was “no” statistical relationship between the number of risk factors associated with the occurrence of PTB in the context of previous pregnancies and demographic variables, except for the mother’s age ($p< 0.05$) (Table **4**).

There was a statistically significant association between the mother's and father's education and the number of PTB risk factors (in both cases, $p < 0.05$). Also, there was a statistically significant relationship between the family's monthly income and the number of PTB risk factors ($p<0.05$). However, there was no statistical relationship with other demographic variables (Table **5**).

4. DISCUSSION

The birth of a preterm infant is one of the serious complications of obstetrics, and prematurity is considered one of the risk indicators for infant death in any society. Various maternal factors have been associated with this phenomenon. Knowledge of these maternal PTB risk factors can guide to eliminate or reduce the impact of such factors. The present study was conducted to determine the maternal factors commonly accompanying PTB in the south of Iran. In this study, the most frequent factors associated with PTB were mothers and fathers with a primary level education, mothers with a housewife occupation, fathers with a farmer/rancher occupation, parental residence in a village, an unwanted pregnancy, maternal hemoglobin less than 11, higher Body Mass Index, pre-eclampsia, gestational diabetes, opium use, and history of cesarean. There was a statistically significant relationship between the number of PTB risk factors and the mother's and father's education and monthly family income.

We found the frequency of low education in parents of premature infants to be very high. Similarly, Enayat Rad *et al.* [9] and Eshghizadeh *et al.* [10] found that the lower education level of the parents is associated with PTB. Also, a study in Spain found that most cases of premature infants occurred in mothers with only a secondary school level education [11, 12].

Also, we found that most mothers of PTBs were housewives, and most fathers were in agriculture and animal husbandry in this rural region of Iran. Those in more urban areas likely had better access to medical facilities than those in rural areas. These families also likely had a higher level of awareness regarding PTB risk, a higher level of health literacy, easier access to information and health education, and finally, the possibility of receiving more advanced care.

Our work supports prior study findings. Enayat Rad *et al.* [9] found that the chance of a PTB in rural areas was higher than in the city. Also, Zhang *et al.* [13, 14] and Eshghizadeh *et al.* [10] found that women who live in the city have a lower chance of a PTB. Other studies found that people who live in rural areas are more prone to PTB due to difficult working conditions and difficult access to health services [15 - 17]. Our PTB cohort had a high frequency of unwanted pregnancies. A case-control study in Gonabad showed that unwanted pregnancy significantly increases the chance of PTB [10]. Gonabad also showed that the low economic level significantly increased the chance of PTB [10], as found in our study.

We also found that anemia was high among women who had PTBs, and this was consistent with the study of Smith *et al.* [18].

We also found that an elevated body mass index was common among women with a PTB; this is consistent with the results of Enayat Rad *et al.*'s study [9], which found a significant relationship between body mass index and premature infants. They found that very thin and fat women have a higher chance of giving birth to a preterm infant. In this regard, Schummers *et al.* found that pre-pregnancy weight loss counseling and achievable weight loss goals for patients could reduce PTB risk [19]. The results of Jafari *et al.*'s study [20] are inconsistent with this finding of the present study, as they did not find a significant relationship between body mass index and PTB. The different results may be due to a different age classification scheme and population social and cultural differences.

We found that preeclampsia was high among PTB mothers with a preterm infant, similar to the pre-eclampsia findings of Shulman *et al.* [21] and the hypertension findings of Fuchs *et al.* [22]. Similar to our study, Enayat Rad *et al.* [9] found that a mother's illness was associated with a higher PTB risk. Conversely, in an urban setting, Davari *et al.* [23] demonstrated a significant relationship between maternal illness and PTB in Tehran. This difference in findings could be due to the difference in urban *versus* rural access to care and types of illness in those settings during pregnancy.

We found that gestational diabetes is common among rural Iranian women with PTBs. These findings suggest that greater attention to managing diabetes could reduce the risk of PTBs. Hawryluk *et al.* found gestational diabetes to be associated with increased congenital disabilities at birth, disruption of intrauterine growth of the fetus, a higher incidence of premature infants, and a higher percentage of intrauterine fetal death [24]. Also, Xie *et al.*, in a meta-analysis study, found that gestational diabetes was associated with a higher incidence of cesarean births, hypertension or preeclampsia, premature rupture of membranes, premature infants, neonatal asphyxia, and polyhydramnios [25].

We found that smoking was higher in mothers with a PTB, and this finding is in line with other related studies [26, 27]. Also, Wallace *et al.* found that smoking has a strong relationship with preterm birth, and quitting smoking can greatly reduce this risk [28]. Ion *et al.* found that PTBs and smoking were linked through mechanisms including vasoconstriction caused by nicotine, fetal hypoxia caused by carbon monoxide, cadmium disruption in calcium signaling, changes in steroid hormone production, disruption in prostaglandin synthesis, and vascular changes in response to oxytocin. The relative importance of each of these pathways has not yet been determined, and further research is necessary to explore the mechanisms through which smoking exerts its effects on pregnancy length and the birth process [29]. Although Dadipour *et al.* found an association between PTB and drug addiction [30], the small number of subjects admitting to addiction precluded us from evaluating this factor effectively in our study.

We found the history of cesarean section in previous pregnancies to be high in mothers with a PTB, consistent with other studies. Leal *et al.* found a high rate of PTB to be associated with previous cesarean deliveries [31].

The limitations of the retrospective cohort study design require caution when assigning causality of common factors to PTB. Also, we did not specifically study the nutritional status of the mothers during pregnancy. Maternal (and fetal) health is likely closely related to the mother's nutritional status. Also, we may have only incomplete information related to substance addiction, domestic violence and smoking, as some women may have been reluctant to share historical information on these topics. Further, a comparison of women of similar age from the same region and time frame without PTB would be helpful for doing a more sensitive case-control analysis.

CONCLUSION

Spontaneous premature infants were common in socially vulnerable groups, such as rural residents or people with low education and a poor economic situation. It is emphasized that reducing social and health inequalities will likely reduce premature birth rates.

AUTHORS' CONTRIBUTIONS

RF, MN, and MA contributed to the concept, design, literature search, data acquisition, and manuscript editing. RR and VM contributed to the data analysis, statistical analysis, and manuscript editing. SD supervised and reviewed the manuscript. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

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HUMAN AND ANIMAL RIGHTS

No animals were used in this research. All procedures performed in studies involving human participants were in accordance with the ethical standards of institutional and/or research committees and with the 1975 Declaration of Helsinki, as revised in 2013.

CONSENT FOR PUBLICATION

Informed consent was obtained from all participants.

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STANDARDS OF REPORTING

STROBE guideline has been followed.

AVAILABILITY OF DATA AND MATERIALS

The data supported the findings of this study will be available upon request for the corresponding author [S.D].

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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