Effects of Delivery Method on Skin Diseases and Allergy Status Depending on Sociodemographic Characteristics

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Abstract

Background Recent data support a relationship between gut microbiota and various chronic diseases, with emerging evidence indicating a similar association with skin microbiota. This study examined the impact of delivery method on skin microbiota and explored its effects on skin diseases and allergies. Sociodemographic characteristics, which are potential factors impacting skin microbiota, were also considered to investigate this relationship. **Methods** A cross-sectional study was conducted with 285 pediatric patients. The delivery method, allergy status, age, gender, consanguineous marriage and parental smoking exposure factors were questioned. The present diagnoses of the patients were also recorded. Categorical variables were analyzed using chi-square analysis and a binary logistic test was used for further analysis. **Results** An increased risk of infectious skin diseases (viral, bacterial, fungal) and allergies has been observed in cesarean section ($p<0.001$, $p=0.057$). The risk of scabies was higher in normal delivery ($p=0.032$). There was no significant relationship between the method of delivery and atopic or non-atopic dermatitis. For children born by cesarean section, parental smoking exposure and allergies were identified as factors increasing the risk of atopic dermatitis ($p=0.045$, $p=0.018$). Allergic children born by cesarean section exhibited a lower prevalence of infectious skin diseases ($p=0.037$). In addition, a decrease in infectious skin diseases from 21,2% to 10,3% was observed after 3 years of age in normal births ($p=0,139$). **Conclusions** Minimizing sociodemographic risk factors and creating a balanced and healthy microbiota, especially in early life, through personal and environmental measures, will be an important part of the treatment of skin diseases and allergies.

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Ethical Approval This study was conducted in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Kirsehir Ahi Evran University (Date: 04.04.2023/ No:2023-07/48).

Data availability The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Methods A cross-sectional study was conducted with 285 pediatric patients. The delivery method, allergy status, age, gender, consanguineous marriage and parental smoking exposure factors were questioned. The present diagnoses of the patients were also recorded. Categorical variables were analyzed using chi-square analysis and a binary logistic test was used for further analysis.

Results An increased risk of infectious skin diseases (viral, bacterial, fungal) and allergies has been observed in cesarean section ($p<0.001$, $p=0.057$). The risk of scabies was higher in normal delivery ($p=0.032$). There was no significant relationship between the method of delivery and atopic or non-atopic dermatitis. For children born by cesarean section, parental smoking exposure and allergies were identified as factors increasing the risk of atopic dermatitis ($p=0.045$, $p=0.018$). Allergic children born by cesarean section exhibited a lower prevalence of infectious skin diseases ($p=0.037$). In addition, a decrease in infectious skin diseases from 21,2% to 10,3% was observed after 3 years of age in normal births (p=0,139).

Conclusions Minimizing sociodemographic risk factors and creating a balanced and healthy microbiota, especially in early life, through personal and environmental measures, will be an important part of the treatment of skin diseases and allergies.

Key Message

In the pediatric age group, the method of delivery and certain sociodemographic characteristics play a crucial role in shaping the gut and skin microbiota. Disruption in the microbiota can impair its physical and immunological functions, potentially leading to a range of diseases. This study suggests that the risk of infectious skin diseases (viral, bacterial, fungal) and allergies is higher in cesarean births, and parental smoking exposure increases the risk of atopic dermatitis in children born by cesarean section.

Main Text

Introduction

The rise in cesarean deliveries and evolving disease patterns necessitate comparing conditions in individuals born through normal vaginal delivery (NVD) and cesarean section (CS). The shift in delivery preferences has prompted recent research, particularly in the past few decades, exploring the connection between the increased occurrence of atopic and allergic diseases and the chosen method of delivery.

Multiple studies have examined the link between delivery method and atopic-allergic diseases (e.g., asthma, allergic rhinitis, atopic dermatitis, food allergy). CS is commonly identified as a risk factor for them [1, 2]. Additionally, some studies propose that CS could also increase the risk of immune-related conditions like inflammatory bowel diseases, immune deficiencies, and connective tissue disorders [3].

Microbiota play crucial roles in shaping the immune system, defending against pathogens, and forming a protective barrier [4]. However, if the microbiome balance is disrupted (known as dysbiosis), these functions can be affected, leading to various disorders. Extensive research has focused on the connection between dysbiosis of gut microbiota and chronic conditions like inflammatory bowel disease, endocrine disorders, and neurodegenerative diseases [5, 6]. But, microorganisms also form the skin microbiota, acting as a protective barrier and influencing the immune function of the skin [7]. Imbalances in the commensal bacteria of the skin microbiota can alter the number and diversity of microorganisms on the skin. Consequently, this disruption can impair the skin's physical and immune barrier functions, potentially leading to the development of skin disorders.

Studies on the relationship between skin microbiota and diseases have increased recently, paralleling the research on gut microbiota. Diseases such as atopic dermatitis (AD), seborrheic dermatitis, acne vulgaris, rosacea, and infectious skin diseases (ISD) have been the focus [7, 8]. Considering the shared immune response system influenced by gut and skin microbiota, it is more accurate to assess their effects on diseases together. The significance of the gut-skin axis is evident in conditions like AD associated with food allergy, dermatitis herpetiformis linked to celiac disease, and psoriasis related to gluten intolerance [8]. Therefore, the interaction between the skin and gut is likely modulated by the common host immune system.

Both skin and gut microbiota can be affected by various factors such as age, gender, genetic structure, chronic disease status, diet, drug use, method of delivery, etc. [9]. The method of delivery is one of the most important factors. Infants delivered via CS are primarily colonized by commensal skin bacteria (such as Staphylococcus, Streptococcus, Corynebacterium, and Propionibacterium), while infants born vaginally acquire organisms from the vaginal flora (including Lactobacillus, Prevotella, Sneatia, Corynebacterium, and Candida albicans) [10]. These microbiota variations, based on exposure to the mother's birth canal microflora, impact the Th1/Th2 balance and the anti-inflammatory cytokine response through interactions between bacterial/viral components and immune cell structures [11]. Consequently, besides the local and physical effects of microbiota composition, altered immune responses can lead to chronic systemic inflammatory conditions. This highlights how the delivery method, including microbiota, can contribute to a wide range of diseases.

Existing studies have primarily focused on exploring the link between delivery method and allergic diseases, leaving a research gap regarding its association with skin diseases. In this study, a unique approach is taken by investigating the impact on skin diseases while simultaneously considering sociodemographic factors that can influence the skin microbiota, in conjunction with the delivery method.

Materials and Methods

This cross-sectional prospective study included 285 pediatric patients under the age of 10 from Kirsehir Training and Research Hospital's dermatology outpatient clinic. Participation was voluntary, and informed consent was obtained from all parents. A questionnaire was administered to gather information on age, gender, consanguineous marriage (CM), family history of smoking, allergy-atopy status, and delivery methods.

Only patients with a confirmed diagnosis of allergy-atopy, supported by the hospital information system, were included.

The study examined both antenatal and postnatal smoking exposure in relation to the family history of smoking. Parents who did not take sufficient precautions to avoid smoking in the presence of their children were categorized as parental smoking exposure (PSE).

The dermatologist recorded the current diagnoses of the patients. Along with addressing their specific concerns, patients underwent a comprehensive systemic dermatologic examination. Patients with additional dermatological diagnoses apart from the main diagnosis were excluded from the study.

Other dermatitis group diseases (seborrheic dermatitis, irritant contact dermatitis, nummular dermatitis, napkin dermatitis, neurodermatitis, and photocontact dermatitis), which do not contain any allergic and atopic components, were grouped as "non-atopic dermatitis (NAD)".

All bacterial, viral, and fungal skin infections were grouped together as ISD. On the other hand, scabies, which is slightly higher in number, was examined separately.

Efforts were made to minimize factors that could impact the flora. As a result, individuals who underwent emergency CS for any reason, experienced birth complications, or received antepartum or intrapartum antibiotics were excluded from the study. Non-inclusion criteria also involved individuals who did not breastfeed for at least 6 months and those with a chronic disease in either the mother or child.

Dermatological diagnoses and allergy status were compared in children born via NVD and CS, considering sociodemographic characteristics.

Data analysis was performed using the SPSS 25.0 package program. Qualitative data were presented as numbers and percentages, while quantitative data were expressed as means with standard deviation. Chi-square analysis was used to assess differences between categorical variables. Further analysis of group differences was conducted using binary logistic regression. Statistical significance was set as $p<0.05$.

Results

The mean age of 285 pediatric patients was 5.25 ±2.92. The youngest patient was 4 months old and the oldest one was 10 years old. Statistical data on gender, age, CM, PSE, method of delivery, allergy status and dermatological diagnoses are presented in Table 1.

58 patients were found to have allergies related to pollen, dust, food, drugs, bee stings, allergic asthma, or allergic rhinitis. In the NAD group of 59 patients, there were diagnoses of seborrheic dermatitis, irritant contact dermatitis, nummular dermatitis, napkin dermatitis, neurodermatitis, and photocontact dermatitis.

34 (11,9%) patients had a viral infection (molluscum or verruca vulgaris), 14 (4,9%) patients had impetigo, 18 (6,3%) patients had tinea or candida which were grouped as ISD. The "other diseases" group included patients with vitiligo, nevus, urticaria, acne vulgaris, hemangioma, and pityriasis alba.

Table 2 presents statistical data comparing delivery method and diagnoses. Accordingly, allergy diagnoses were 3.3 times higher in those born by CS ($p<0.001$, 95% CI=1.695-6.472). No significant difference was found in both AD and NAD groups. However, scabies was found to be 2.4 times higher in those born by NVD (p=0,032, 95% CI=1,057-5,444). It was also noted that ISD were more common in those born by CS (p=0,057).

Comparison of AD status in NVD and CS groups according to sociodemographic characteristics is shown in Table 3. Accordingly, the risk of AD was found to be significantly higher in children with PSE who were born by CS (p=0,045). It was also observed that allergic children had a risk for AD in both NVD (p=0,076) and CS (p=0,018), but this risk was 3.1 times higher in CS delivery (p=0,038, 95% CI= 1,065-9.139).

Table 4 illustrates the comparison of NAD status in the NVD and CS groups based on sociodemographic characteristics. The results indicate that PSE reduces the risk of NAD in children born by NVD (p=0,051).

According to the ISD comparisons in Table 5, the risk of ISD was lower in children born by CS whose parents were consanguineous (p=0,080). Notably, the rate of ISD in the 0-3 age group in normal-born children decreased from 21,2% to 10,3% in children over 3 years of age (p=0,139). Additionally, CS-born allergic children showed a lower prevalence of ISD (p=0.037).

Sociodemographic characteristics and allergy status did not significantly impact the occurrence of scabies in both normal and cesarean deliveries. No significant relationship was found between sociodemographic characteristics and allergy status based on the mode of delivery.

Discussion

In recent studies, the relationship between delivery methods and atopic-allergic diseases has gained increased attention. Asthma, allergic rhinoconjunctivitis, AD, and food allergies have been extensively studied in this context [1, 2]. In a meta-analysis conducted by Bager et al. with 26 studies, it was observed that CS moderately increases the risk of allergic rhinitis, asthma, and food allergy, but not inhalant atopy or AD [12].

In our study, patients with various allergies were grouped together due to a low number of patients in each subtype. Comparing the delivery method and allergic conditions, it was found that CS birth carried a 3.3 times increased risk of developing allergies (Table 2). Although the precise mechanisms underlying this relationship are still not clarified, it is clear that the early formation and maturation of the infant microbiome has a significant impact on immune system development and prevention of allergic diseases.

Some studies suggest a link between delivery method and AD [13], but most studies have not found conclusive evidence to support this association [12, 14, 15]. Ofcourse, factors such as genetics, environment, age, and sociodemographic characteristics may influence this relationship. In our study, no significant association was found between delivery method and AD (p=0.864) (Table 2).

Sociodemographic characteristics and allergy status were also analyzed in normal and cesarean births separately for their impact on AD (Table 3). Herein, PSE showed a significant association with increased AD in CS (p=0.045). Literature suggests that active smoking and passive smoke exposure are linked to higher AD prevalence in children and adults [16]. Smoking likely contributes to AD indirectly by disrupting the microbiota, in addition to its direct effects on the immune system and skin barrier. Consequently, it can be concluded that PSE in CS-born patients may enhance AD susceptibility by influencing the microbiota, immune system, or underlying mechanisms.

In our study, it was observed that having allergies increased the risk of AD in both normal and CS delivery, but this risk was 3.1 times higher in CS (p=0.038, 95% CI=1.065-9.139) (Table 3). The mechanism behind AD is not fully understood, but factors such as gene interactions, skin barrier defects, infectious agents, host environments, and immunological responses are believed to play a role [17]. Recent research emphasizes the importance of allergens in AD [18]. The skin's immune response to allergens in AD involves complex processes, including both immediate IgE-mediated and delayed T-cell-mediated responses [19]. In this intricate mechanism influenced by multiple factors, a balanced microbiota associated with NVD seems to partially mitigate the occurrence of AD in individuals with allergies.

The study found that the delivery method had no effect on NAD similar to AD (p=0.923) (Table 2). However, unlike AD, allergy did not impact NAD, and NAD cases were less common in normally born children exposed to parental smoke (Table 4). This unexpected effect of smoking on NAD contradicts existing literature, which indicates that smoking irritates the skin due to toxic substances and disrupts blood flow and skin oxygenation [20]. Although this result may be influenced by the limited number of patients in the study, it is worth investigating the distinct effects of smoking on the microbiota of normal and cesarean-born children through non-atopic pathways.

ISD was more common in patients born by CS (p=0.057) (Table 2). Conversely, scabies cases were significantly more prevalent in those born by NVD (p=0.032) (Table 2). The association between the ISD and CS may be linked to disrupted microbiota and compromised immune response. However, distinct factors need

to be considered for the scabies group. The higher incidence of scabies in NVD births could be attributed to differences in the mechanism of parasitic diseases or the presence of unique sociodemographic characteristics among those opting for normal birth, potentially leading to living in less hygienic and more crowded environments.

The infection rate in both the 0-3 and 3+ age groups was similar and high in CS, but it decreased from 21.2% to 10.3% in NVD (Table 5). Studies on the gut microbiota indicate significant changes until the age of 2-3 years [21]. Zhu et al. demonstrated that the delivery method continues to affect skin microbiota even up to 10 years of age [22]. In this study, the decrease in cases of ISD among the 3+ age group born via NVD may be attributed to the gradual development of the microbiome, enhancing its physical and immunological protective functions over time. The elevated ISD rate in CS up to 10 years of age (26.8%) is likely due to the long-term impact of altered microbiota.

Allergies were found to be associated with a decreased risk of ISD in patients delivered by CS (p=0.037) (Table 5). The exact immunological mechanism is unknown, but it is worth noting that attentive care provided to allergic children born via CS and their upbringing in a hygienic environment may have contributed to these results. Additionally, although not statistically significant, CM appears to decrease the risk of ISD in CS (p=0.080). It is important to consider that besides systemic and local factors, genetic and sociodemographic factors, as well as the limited number of patients, may have influenced these results.

The high risk of ISD and allergies in CS reveals the importance of a balanced and healthy microbiota in the postpartum period. Taking into consideration the systemic, local, and immunological impacts of the microbiota, it can be inferred that the microbiota could play a crucial role as an etiological factor in a broad range of diseases. It is also crucial to consider that certain sociodemographic characteristics can have an impact on the microbiota.

Among so many factors, it is necessary to develop patient-specific treatment methods rather than disease. In addition to the standard treatments for diseases, establishing a balanced and healthy microbiota, particularly during early childhood, and maintaining its stability through personal and environmental measures will constitute a significant aspect of the treatment.

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Tables

Table 1 Characteristics of the patients

			N	%
Gender	Male	Male	147	51.6%
	Female	Female	138	48.4%
Age	0-3	0-3	205	71.9%
	>3	>3	80	28.1%
CM	Yes	Yes	46	16.1%
	No	No	239	83.9%
PSE	Yes	Yes	143	50.2%
	No	No	142	49.8%
Mode of Delivery	Normal	Normal	124	43.5%
	Cesarean	Cesarean	161	56.5%
Allergy	has		58	20.4%
	not		227	79.6%
Dermatological Diagnosis	AD	AD	75	26.3%
	NAD	NAD	59	20.7%
	ISD[a]	ISD[a]	66	23.2%
	Scabies	Scabies	27	9.5%
	Other Diseases	Other Diseases	58	20.4%

[a] ISD includes viral, bacterial and fungal skin infections. *CM* Consanguineous Marriage, *PSE* Parental Smoking Exposure, *AD* Atopic Dermatitis, *NAD* Non-atopic Dermatitis, *ISD* Infectious Skin Diseases

Table 2 Comparisons of delivery methods and diagnoses

	Normal	Normal	Cesarean	Cesarean	*P*-value

		n	%	n	%	
Allergy	has	13	10,5%	45	28,0%	<0,001
	not	111	89,5%	116	72,0%	
AD	has	32	25,8%	43	26,7%	0,864
	not	92	74,2%	118	73,3%	
NAD	has	26	21,0%	33	20,5%	0,923
	not	98	79,0%	128	79,5%	
ISD[a]	has	22	17,7%	44	27,3%	0,057
	not	102	82,3%	117	72,7%	
Scabies	has	17	13,7%	10	6,2%	0,032
	not	107	86,3%	151	93,8%	

[a] ISD includes viral, bacterial and fungal skin infections. *AD* Atopic Dermatitis, *NAD* Non-atopic Dermatitis, *ISD* Infectious Skin Diseases

Table 3 Comparisons of atopic dermatitis status in normal and cesarean delivery groups according to sociodemographic characteristics

		Normal Delivery Atopic Dermatitis has	Normal Delivery Atopic Dermatitis has	Normal Delivery Atopic Dermatitis not	Normal Delivery Atopic Dermatitis not	Normal Delivery Atopic Dermatitis	C A I
		n	%	n	%	*P*-value	n
Gender	Female	13	21,3%	48	78,7%	0,260	2
	Male	19	30,2%	44	69,8%		1
Age	0-3	19	22,4%	66	77,6%	0,194	3
	>3	13	33,3%	26	66,7%		9
CM	Yes	8	29,6%	19	70,4%	0,608	4
	No	24	24,7%	73	75,3%		3
PSE	Yes	19	29,7%	45	70,3%	0,308	2
	No	13	21,7%	47	78,3%		1
Allergy	has	6	46,2%	7	53,8%	0,076	1
	not	26	23,4%	85	76,6%		2

CM Consanguineous Marriage, *PSE* Parental Smoking Exposure

Table 4 Comparisons of non-atopic dermatitis status in normal and cesarean delivery groups according to sociodemographic characteristics

		Normal Delivery Non-atopic Dermatitis has	Normal Delivery Non-atopic Dermatitis has	Normal Delivery Non-atopic Dermatitis not	Normal Delivery Non-atopic Dermatitis not	Nor Non
		n	%	n	%	*P*-v
Gender	Female	14	23%	47	77%	0,59
	Male	12	19%	51	81%	
Age	0-3	18	21,2%	67	78,8%	0,93
	>3	8	20,5%	31	79,5%	
CM	Yes	4	14,8%	23	85,2%	0,37
	No	22	22,7%	75	77,3%	
PSE	Yes	9	14,1%	55	85,9%	0,05
	No	17	28,3%	43	71,7%	
Allergy	has	1	7,7%	12	92,3%	0,29

not	25	22,5%	86	77,5%	

[a] These have at least 1 cell with an expected count of less than 5. Therefore, the P-value obtained from Fisher's Exact Test took precedence over Pearson's Chi-square. *CM* Consanguineous Marriage, *PSE* Parental Smoking Exposure

Table 5 Comparisons of infectious skin diseases (viral, bacterial, fungal) in normal and cesarean delivery groups according to sociodemographic characteristics

		Normal ISD has	Normal ISD has	Normal ISD not	Normal ISD not	Normal ISD	Cesarean ISD has	Cesarean ISD has	Cesarean ISD not	Cesarean ISD not	Cesare ISD
		n	%	n	%	*P*-value	n	%	n	%	*P*-valu
Gender	Female	10	16,4%	51	83,6%	0,699	18	23,4%	59	76,6%	0,281
	Male	12	19%	51	81%		26	31%	58	69%	
Age	0-3	18	21,2%	67	78,8%	0,139	33	27,5%	87	72,5%	0,934
	>3	4	10,3%	35	89,7%		11	26,8%	30	73,2%	
CM	Yes	6	22,2%	21	77,8%	0,570[a]	2	10,5%	17	89,5%	0,080
	No	16	16,5%	81	83,5%		42	29,6%	100	70,4%	
PSE	Yes	14	21,9%	50	78,1%	0,213	19	23,8%	61	76,3%	0,311
	No	8	13,3%	52	86,7%		25	30,9%	56	69,1%	
Allergy	has	1	7,7%	12	92,3%	0,461[a]	7	15,6%	38	84,4%	0,037
	not	21	18,9%	90	81,1%		37	31,9%	79	68,1%	

[a] These have at least 1 cell with an expected count of less than 5. Therefore, the P-value obtained from Fisher's Exact Test took precedence over Pearson's Chi-square. *ISD* Infectious Skin Diseases, *CM* Consanguineous Marriage, *PSE* Parental Smoking Exposure