**RESULTS**

**Study Population and Prevalence of Congenital Hypothyroidism** (**CH)**

Between 2008 and 2017, there were a total of 19,533 births in the Negev region in southern Israel. Of these, 131,350 (67.2%) were among the Bedouin population and 63,983 (32.8%) were among the Jewish population. Data obtained from the Soroka Medical Center in the city of Beersheva and from the newborn screening survey indicated that there were 106 children born with congenital hypothyroidism (CH) among these Bedouin and Jewish populations. A comparison of the prevalence of CH in the Bedouin and Jewish populations in the Negev between 2008-2017 showed a significant difference in prevalence: among Jews, the rate was 0.073%, whereas, among the Bedouin population, it was 0.045% (p-value < 0.01) as shown in Table 1.

**Predictors of CH: Univariate Analyses**

An overall summary of the results shows a significant relationship (CI 95% 1.002-4.792) between gender and the prevalence of CH among the Bedouin and Jewish populations. In the Jewish population, the prevalence of this disease was higher among females (61.7%) than among males (38.3%), whereas among the Bedouin population, the prevalence was lower among females (42.45%) than males (57.6%).

Looking at the factor of residence revealed that among the Jewish population, CH was more prevalent among newborns from the urban area (74.5%) as compared to those from a kibbutz or small township (25.5%). Among the Bedouin community, the disease was more prevalent among newborns from dispersed settlements (39.0%) as compared to those from permanent settlements (32.2%). These results are not surprising, and may be attributed to the nature of the living conditions among these different populations in Israel.

Furthermore, a significant correlation (p-value < 0.001) was found between socioeconomic status (SES) and the prevalence of this disease. In general, the Jewish population has a higher income than the Bedouin population. In Jewish newborns (+5.26-3.307, Bedouin newborns +2.02-1.37). Moreover, a correlation was found between the prevalence of this disease among babies born to mothers who smoke cigarettes. Bedouin mothers who smoke are more likely to have children with CH (29.8%) as compared to 0% among children of Jewish mothers who smoke.

Analysis of the relationship between gender and ethnic background among children with CH revealed that there is a risk of 2.191 (CI 1.002-4.792). Among the Bedouin population, the prevalence of CH is higher among males (57.6%) than females (~~38.3%~~ 42.4%). In contrast, among Jews, the disease is more prevalent among females (61.7%) than males (~~42.4%~~ 38.3%), as shown in Table 2.

The current study found a significant correlation between CH and various disease etiologies (p-value < 0.001). The various types of dyshormonogenesis are more common among the Bedouin population (23.7%), whereas among the Jewish population, other etiologies (“unknown”) are more common, at a rate of 44.7%, followed by thyroid dysgenesis at 27.7%. Examination of the relationship between each individual etiology and ethnic background showed a relationship between the etiology of dyshormonogenesis and ethnic background, specifically that the OR 0.219 is significantly in the direction of the Jewish community (CI 0.059-0.816), meaning that dyshormonogenesis increases the risk of the disease in the Bedouin population. Additionally, it was found that among the Bedouin population, the etiology of Down syndrome significantly increases the risk of CH (CI 0.425-0.625), OR 0.515 in the direction of the Jewish community.

When considering unidentified etiologies, there is a significant relationship (CI 0.425-0.625), but the risk increases in the Jewish population (OR 2.596). The current study also found a significantly higher incidence of additional congenital defects among the Bedouin population (71.2%) as compared to the Jewish population (40.5%) as shown in Table 3.

**Predictors of CH in Multivariate Analyses**

A multivariate analysis model applied to the entire study population found that a mother with hypothyroidism (CI 95%: 1.040-4.402) has a significantly higher risk of giving birth to a baby with CH, as compared to a mother who does not suffer from the disease (adjusted OR 2.140). However, when we applied the multivariate analysis model to each subpopulation separately, it was found that in the Bedouin population, maternal hypothyroidism increases the risk of CH in newborns, [adjusted OR] 4.076), whereas among the Jewish population, maternal hypothyroidism was not found to significantly increase the risk of the disease in their children.

**Discussion**

In this retrospective study comparing Jewish and Bedouin populations, the main findings contradicted our hypothesis that the disease would be more prevalent in the Bedouin population than in the Jewish population. Instead, this study found that the prevalence of CH among children born in the Negev between 2008-2017 was higher among the Jewish population (0.073%) than among the Bedouin population (0.045%). These results are consistent with another study conducted in Israel between 2011-2015, which found that the prevalence of the disease is higher among Jews than among the Arab population (1). This raises the question of whether there is a genetic link causing a predisposition towards CH among the Jewish population, and/or if Bedouin ancestry is a protective factor against this disease.

In addition, the analysis identified several variables that are correlated with ethnic background in influencing the prevalence of the disease. First, a relationship was found between gender and ethnic origin in the prevalence of CH, namely that among the Bedouin population the incidence is higher among males, while in the Jewish population, it is higher among females.

A previously conducted meta-analysis also found that this disease is more prevalent among females than males (2). Similarly, a previous newborn survey in Israel found the prevalence of CH to be higher among females than males (1). This corresponds to the findings of our survey regarding the Jewish population. However, the higher incidence of CH among male newborns compared to females in the Bedouin population does not correspond to the literature. A possible reason for these findings is information bias since this is a retrospective study.

We found little literature showing a clear relationship between gender and incidence of the disease, but it is known that thyroid hormone plays an important role in the development of the reproductive system and in maintaining reproductive function for both males and females.

Furthermore, a relationship was found between SES and the incidence of the disease. While SES among the Jewish population is higher than among the Bedouin population, the incidence of the disease is higher among the Jewish population. This finding contradicts the results of a previous study conducted in Israel, which found that the disease is more common among those in a higher socioeconomic level (1). This difference could be due to the sample size. The current study examined only the population of the Negev, whereas the previous study considered the entire population in Israel; therefore, another possible reason for these findings is the unique genetic composition of the population in the Negev.

It is important to note that SES has an impact on the prognosis of a child with this disease; children from lower SES have a poorer prognosis. Previous studies have found that lower SES is associated with delayed diagnosis of CH, and late diagnosis may negatively affect the child's development and intellectual abilities (3). This may be due to barriers such as a lack of access to medical care and diagnostic tests. This emphasizes the importance of addressing disparities in health care and ensuring that all children have access to timely and appropriate medical care.

Our study also found that the incidence of this disease among newborns is higher among Bedouin mothers who smoke than among Jewish mothers who smoke.

When we looked at the etiologies of the disease, it was found that in the Bedouin population, dyshormonogenesis is the most common (CI 95% 0.059-0.816), followed by “unknown etiology” and Down syndrome. Among the Jewish population, the most common is “unknown etiology” followed by dyshormonogenesis. The study did not find a clear connection between thyroid dysgenesis and an increased prevalence of CH in either of the populations. According to the literature, most cases of CH are thyroid dysgenesis (16).

Congenital hypothyroidism (CH) is a condition that affects the development of the thyroid gland, causing reduced thyroid function from birth. There is evidence indicating a possible connection between CH and other congenital defects in newborns. For example, a study found a higher level of additional congenital defects among children with CH from the Bedouin population, as compared to the Jewish population; that is, in the Jewish population children with CH are less likely to have other congenital defects. The most common congenital diseases associated with CH in the Bedouin population of Israel are Down syndrome and heart disease; this finding is similar to those of studies conducted in Italy (4) and Western Iran (5). The reasons for a correlation between CH and other birth defects are unclear but may be related to underlying genetic and developmental factors, which may have caused both conditions. In addition, CH can negatively impact other organ systems and metabolic pathways, which may contribute to the increased risk of other congenital abnormalities.

Analysis of the results indicated a positive correlation between CH and siblings who have hypothyroidism; that is, newborns who have siblings with this disease are more likely to have it themselves. Although the p-value was 0.062, this could be due to the size of the study population, and if a larger population had been examined, a stronger relationship may have been found.

A multivariate analysis of the entire population found that hypothyroidism in the mother increases the risk of the disease in the newborn. Analysis of the entire population covered in this study, which included newborns with transient congenital hypothyroidism and those with permanent congenital hypothyroidism, found that mothers with hypothyroidism have a higher chance of giving birth to children with transient CH. This is consistent with previous literature (17). However, a multivariate analysis of the Jewish population alone did not identify any factor that significantly increases the risk of the disease. This is important, because thyroid hormones are necessary for fetal growth and development, and a lack of thyroid hormones during pregnancy may affect the development of the fetal brain and other organs. Maternal hypothyroidism can be caused by several factors, including autoimmune thyroid disease, iodine deficiency, or previous thyroid surgery. Early identification of risk factors can allow for early treatment and prevention of later complications.

**Study Limitations**

This study had a number of limitations. Since it is a retrospective study, data for some patients was missing in the medical records. There was difficulty in obtaining external validity. The composition of the population in the Negev makes it difficult to generalize the findings to the entire population of Israel. In the Negev, about 50% of the births are in the Bedouin population, among whom marriages between close relatives are common, whereas, among the Arab populations in other parts of Israel, this practice is less common.

The strengths of the study were that the data were collected from the Soroka Hospital, a large hospital in which most of the births from families in the Negev region take place. In addition, most patient follow-ups are conducted in this hospital, so there is a high level of organization and continuity among the data.

**Conclusion**

The main conclusion of this study is that in the Negev, the prevalence of CH is higher among the Jewish population than among the Bedouin population, which contradicted our hypothesis that the disease would be more common among the Bedouin population. The initial data analysis showed that within the population of patients with CH, there were indeed more cases among those from the Bedouin community, which explains our mistaken hypothesis. However, analysis of the frequency of CH among the total number of births at Soroka Hospital revealed the unexpected statistic that the frequency is in fact higher among the Jewish population. This suggests the need for further research examining whether there is a genetic risk factor for the disease among the Jewish population, and conversely, whether there is a genetic protective factor in the Bedouin community.

Another unexpected finding was the positive correlation between higher SES and higher incidence of the disease. However, given that SES is higher among the Jewish population than the Bedouin population, this relates to the question stated above, namely whether the apparent correlation is, in fact, a result of SES, or whether it reflects the genetic composition of the two populations, which have differing SES.