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ABO & Rh BLOOD GROUP AS A RISK FACTOR OF HYPOTHYROIDISM

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Abstract:

Background: *The clinical significance of the ABO blood group system extends beyond transfusion medicine as several reports have suggested an important involvement in the development of neoplastic and cardiovascular disorders, peptic ulcers, coagulation and infection.* ***Objective:*** *to show the prevalence of hypothyroidism in various ABO and Rh blood group subjects, and to examine the strength of association between hypothyroidism and ABO, Rh blood groups subjects in Arar City, Northern Saudi Arabia.* ***Methods:*** *A cross-sectional study, conducted in Arar city, Northern Saudi Arabia. During the period from 1 January to 31 May 2018. The study included 746 participants. Collected data analyzed using the SPSS program (version 22). P-value of less than 0.05 considered statistically significant.* ***Results:*** *the total prevalence of hypothyroidism was 5.9%. As regards the blood group, blood group O was the most common (44.5%), followed by blood group A (26.7 %) and B (20.8 %), and the least common one was AB (8%). Rhesus factor (Rh) was positive in 86.1% and negative in 13.9%. The majority (86.4%) of hypothyroid patients were females (P value=0.0001). The data show a significant difference in hypothyroidism in the different blood groups (P value= 0.048) with group A subjects of the highest association (8% of group A subjects). Rh blood type had no statistically significant association with hypothyroidism.* ***Conclusion:*** *The results of our study showed a significant difference in hypothyroidism in the different blood groups with group A subjects of the highest association. Our findings support the need for further investigation to look for the association between ABO blood groups and hypothyroidism, further investigations in a larger population are warranted.*

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INTRODUCTION:

Hypothyroidism is a condition caused by the insufficient production of thyroid hormone by the thyroid gland. Factors such as the iodine deficiency or the exposure to Iodine-131 can increase the risk of this disease. It's usually seen when the daily intake of iodine falls below 25µg. Hypothyroidism can be classified according to the gland function into primary and secondary[1].The prevalence of spontaneous hypothyroidism is between 1% and 2%, and it is more common in older women and ten times more common in women than in men[2]. In the Whickham survey, the prevalence of newly diagnosed overt hypothyroidism was 3 per 1000 women[3].

Blood group antigens are rather simple chemical moieties on the red blood cell (RBC) surface whose structure is gradually being elucidated. "Naturally occurring" anti-A and anti-B are bacterial antibodies that coincidentally cross-react with RBCs. The clinical significance of the ABO blood group system extends beyond transfusion medicine as several reports have suggested an important involvement in the development of neoplastic and cardiovascular disorders[4, 5]. The early statistical associations with disease, are those with malignancy, peptic ulcers, coagulation and infection.

In 1954, ***Aird and Bentall*** reported that patients suffering from peptic ulcer show an increased incidence of blood group O (about 35 % more likely to develop peptic ulceration than are persons of the other groups) and a correspondingly lower incidence of the other three blood groups[6]. A study that assessed the association and distribution of hypertension, obesity, and ABO blood groups in different categories of blood donors concluded that the individuals with B blood group were more susceptible to hypertension and obesity[7] . Another study done by ***Aboel-Fetoh et al.*** in Arar city in Saudi Arabia found no association between overweight, obesity, and ABO blood groups or Rh[8].

Some epidemiological studies demonstrated significant association between "ABO" blood groups and the risk of DM. In the study of ***Barbalic et al***.[9], blood group B was associated with a decreased risk of DM compared to blood group O. However, some studies did not find any relationship between blood group and DM[10].

This study was carried out to determine any association between ABO blood groups, Rhesus factor groups "RH" and Hypothyroidism in Arar city, Northern Saudi Arabia. To our knowledge, no similar studies have been done to evaluate this relation in Kingdom of Saudi Arabia.

Objective

The objective of this study was to show the prevalence of hypothyroidism in various ABO and Rh blood group subjects, and to examine the strength of association between hypothyroidism and ABO, Rh blood groups subjects in Arar City, Northern Saudi Arabia.

Participants and Methods:

Study design: A cross-sectional study, conducted in Arar city, Northern Saudi Arabia. During the period from 1 January to 31 May 2018,
The study included 746 participants from the general population of Northern Saudi Arabia.

Data collection: data were collected using a pre-designed online questionnaire, which was distributed among Arar city population. It was self-administered by participants. The questionnaire included the relevant questions to collect data about:

- Socio-demographic characteristics of the participants including age, sex, marital status, working status and educational level
- Body weight and height for calculation of the Body Mass Index (BMI); Weight in Kg/Height in m^2.
- If the participant has, a physician diagnosed hypothyroidism.
- ABO and Rh Blood groups of the participants.

Statistical analysis:

Collected data were coded and analyzed using Statistical Package for the Social Sciences (SPSS, version 22). Descriptive statistics for the prevalence and quantitative variables was used. Strength of association between hypothyroidism and blood groups was determined using the chi-square test. P-value of less than 0.05 considered statistically significant.

Ethical considerations:

The questionnaire included a brief introduction or explanation of the idea and objectives of the research, it also included a consent form to be signed by the participants before filling the required data. Participants were informed that participation is completely voluntary. No names were recorded on the questionnaires and all questionnaires kept safe.

RESULTS:

Table 1 illustrates the sociodemographic characteristics and Body Mass Index (BMI) of the studied population. It is clear from the table that, the females constituted 56.8%, the majority (40.8%) aged 20 – 29 years, and 20.8% aged 40 – 59 years. University or higher education group were 62.9% while 27.5% got secondary education. Single participants constituted 52.7% but married were 44.0%. As regards the Body Mass Index (BMI), underweight 8.2%, overweight 31.1%, obese 26.3% and normal weight population were 34.5%.

Table (2) shows the hypothyroidism, ABO blood group and Rhesus factor (Rh) in the studied population. It is clear from the table that, the total prevalence of hypothyroidism was 5.9%. Ss regards the blood group, blood group O was the most common (44.5%), followed by blood group A (26.7 %) and B (20.8 %), and the least common one was AB (8%). Rhesus factor (Rh) was positive in 86.1% and negative in 13.9%.

Table 3 illustrates the relationship between hypothyroidism and sociodemographic characteristics of the studied population. It is clear from the table that the majority (86.4%) of hypothyroid patients were females (P value=0.0001). The table showed also that most (43.2%) of hypothyroid patients were older (in the age group 40 – 59 years) with a statistically significant value (P value = 0.001). Marital status has a statistically significant value in comparison with hypothyroidism (P value= 0.0001). In the table, no significant difference between the BMI groups and hypothyroidism, however most of our subjects (57.4%) were either overweight or obese. Educational level and working status had no statistically significant association with hypothyroidism. We have found that female gender and diabetes are significant risk factors for hypothyroidism

Table (4) shows the relationship between hypothyroidism and ABO blood group, Rhesus factor (Rh), diabetes mellitus, type of diabetes and hypertension among the studied population. The data show a significant difference in hypothyroidism in the different blood groups (P value= 0.048) with group A subjects of the highest association (8% of group A subjects). We found the prevalence of DM to be 18%, half of them are T1DM. The comparison between hypothyroidism and DM has revealed that DM has a significant association with hypothyroidism (P value= 0.007) and that 11% of our DM patients were hypothyroid. When comparing hypothyroidism with type 1 DM (T1DM) versus T2DM, the former was significantly associated with hypothyroidism (P value= 0.013). Rh blood type and hypertension had no statistically significant association with hypothyroidism.

Table (1): Sociodemographic characteristics of the studied population, Arar, 2018. (N=746)

Variable	No.	%
Gender		
• Male	322	43.2
• Female	424	56.8
Age group		
• < 12 years	3	.4
• 12 – 19 years	126	16.9
• 20 – 29 years	304	40.8
• 30 – 39 years	142	19.0
• 40 – 59 years	155	20.8
• > 60 years	16	2.1
Educational level		
• Primary	30	4.0
• Intermediate	42	5.6
• Secondary	205	27.5
• University or higher	469	62.9
Marital status		
• Single	393	52.7
• Married	328	44.0
• Divorced	16	2.1
• Widow	9	1.2
Working status		
• Yes	298	39.9
• No	448	60.1
BMI group		
• Underweight	61	8.2
• Normal weight	257	34.5
• Overweight	232	31.1
• Obese	196	26.3

Table (2): Hypothyroidism, ABO blood group and Rhesus factor (Rh) in the studied population, Arar, 2018. (N=746)

	Frequency	Percent
Hypothyroidism		
• Yes	44	5.9
• No	702	94.1
ABO blood group		
• A	199	26.7
• B	155	20.8
• AB	60	8.0
• O	332	44.5
Rhesus factor (Rh)		
• Rh +	642	86.1
• Rh -	104	13.9

Table (3) Relationship between hypothyroidism and sociodemographic characteristics of the studied population, Arar, 2018.

Variables	**Responses**	**Hypothyroidism**		**Total (N=746)**	**P value**
		No (N=702)	**Yes (N=44)**		
Gender	Male	316	6	322	0.0001
		45.0%	13.6%	43.2%	
	Female	386	38	424	
		55.0%	86.4%	56.8%	
Marital status	Single	381	12	393	0.0001
		54.3%	27.3%	52.7%	
	Married	300	28	328	
		42.7%	63.6%	44.0%	
	Divorced	14	2	16	
		2.0%	4.5%	2.1%	
	Widow	7	2	9	
		1.0%	4.5%	1.2%	
Age group	<12 years	3	0	16	0.001
		0.4%	0.0%	2.1%	
	12 – 19 years	121	5	3	
		17.2%	11.4%	0.4%	
	20 – 29 years	297	7	126	
		42.3%	15.9%	16.9%	

	30 – 39 years	130	12	304	
		18.5%	27.3%	40.8%	
	40 – 59 years	136	19	142	
		19.4%	43.2%	19.0%	
	>60 years	15	1	155	
		2.1%	2.3%	20.8%	
Educational level	Primary	28	2	30	0.619
		4.0%	4.5%	4.0%	
	Intermediate	41	1	42	
		5.8%	2.3%	5.6%	
	Secondary	195	10	205	
		27.8%	22.7%	27.5%	
	University or higher	438	31	469	
		62.4%	70.5%	62.9%	
Working status	Yes	277	21	298	0.176
		39.5%	47.7%	39.9%	
	No	425	23	448	
		60.5%	52.3%	60.1%	

Table (4): Relation between hypothyroidism and ABO blood group, Rhesus factor (Rh), diabetes mellitus, type of diabetes and hypertension among the studied population.

Variables	**Responses**	**Hypothyroidism**		**Total (N=746)**	**P value**
		No (N=702)	**Yes (N=44)**		
ABO blood group	A	182	17	199	0.048
		25.9%	38.6%	26.7%	
	B	152	3	155	
		21.7%	6.8%	20.8%	
	AB	58	2	60	
		8.3%	4.5%	8.0%	
	O	310	22	332	
		44.2%	50.0%	44.5%	
Rhesus factor (Rh)	Rh+	607	35	642	0.146
		86.5%	79.5%	86.1%	
	Rh -	95	9	104	
		13.5%	20.5%	13.9%	
BMI group	Underweight	59	2	61	0.308
		8.4%	4.5%	8.2%	

	Normal weight	246	11	257	
		35.0%	25.0%	34.5%	
	Overweight	214	18	232	
		30.5%	40.9%	31.1%	
	Obese	183	13	196	
		26.1%	29.5%	26.3%	
Diabetes mellitus	yes	121	15	136	0.007
		17.2%	34.1%	18.2%	
	no	581	29	610	
		82.8%	65.9%	81.8%	
Type of diabetes	Type 1	56	12	68	0.013
		46.3%	80.0%	50.0%	
	Type 2	65	3	68	
		53.7%	20.0%	50.0%	
Hypertension	yes	65	8	73	0.056
		9.3%	18.2%	9.8%	
	no	637	36	673	
		90.7%	81.8%	90.2%	

DISCUSSION:

This study try to determine an association between ABO blood groups and Hypothyroidism in the population of Arar city, Northern Saudi Arabia. Previous literatures lacks information regarding this association in Saudi adults.

Our study found the prevalence of hypothyroidism to be about 5.9%. Saudi Arabia have higher prevalence of hypothyroidism than other countries as evident from previous studies done in Saudi Arabia[8,11].

A previous study was done by ***Rana et al***. in which 199 females participated in the study aged between 20 and 65 years with a mean age of 29.49 years, showed that the incidence rate of hypothyroidism (including subclinical cases) in female Saudi adults visiting the King Khalid University Hospitals, Riyadh was 15.5% [11].

A large prospective study performed in Utah and Arizona, USA in 1965–1968, with patients followed up as adults in 1985 to 1987, showed that hypothyroidism was found in 1.6% of young adults in their 30s. [12].

In our study, 86.4% of hypothyroid patients are female gender (P value=0.0001), this result agreed with previous literature that females have ten times higher risk of hypothyroidisms than males [3].

A comparison of age groups in hypothyroid patients showed that (43.2%) of hypothyroid patients were older (in the age group 40 – 59 years) with a statistically significant value (P value = 0.001). There are plenty of studies showing a higher incidence of hypothyroidism with increasing age [13, 14], with most of cases being in the fifth decade or younger.

In our study, blood group O was the most common (44.5%), followed by blood group A (26.7 %) and B (20.8 %), and the least common one was AB (8%). These figures are comparable to the ABO blood group distribution of Kingdom of Saudi Arabia population in the international survey of racial and ethnic distribution of ABO blood types[15] which reported that the incidence of blood groups was as follows: (52%) for blood group O, (26%) for blood group A, (18%) for blood group B, and (4%) for AB blood group.

Our results show a significant difference in hypothyroidism in the different blood groups **(P value**= 0.048) with group A subjects of the highest association (8% of group A subjects). This finding in hypothyroid patients is reported for the first time in our study.

There are various associations between particular ABO phenotypes and an increased susceptibility to disease [6]. ABO blood groups are associated with some important chronic metabolic diseases such as diabetes mellitus (DM) [7] and malignant diseases such as gastric cancer [8] and pancreatic cancer [9]. Data from large prospective cohort studies indicate that the ABO blood group is associated with the risk of developing skin, ovarian and lung cancers [10-12]. A systematic review and meta-analysis done to evaluate the association between ABO blood groups and overall cancer risk, as well as the risk of individual cancer sites Concluded that Blood group A is associated with increased risk of cancer, and blood group O is associated with decreased risk of cancer, and that in comparing B vs non-B blood groups with cancer thyroid, OR= 1.30 and 95% CI= (1.02- 1.66), which is a significant relation [13].

We found the prevalence of DM to be 18%, half of them are T1DM**.** The overall prevalence of DM in adults in KSA is 23.7% [16]. Saudi Arabia is the seventh of the top ten countries in terms of the prevalence of diabetes among the adult population aged 20–79, according to the IDF diabetes atlas 2012 [17].

The comparison between hypothyroidism and DM has revealed that DM has a significant association with hypothyroidism **(P value= 0.007)** and that 11% of our DM patients were hypothyroid.

Hypothyroidism has been observed to be quite prevalent in patients with diabetes. The prevalence of thyroid dysfunction among Saudi diabetic patients was reported to be 16%, as opposed to 7% in nondiabetics, as shown by ***Akbar et al***. in 2006 [18].Another study about Risk Factors for Thyroid Dysfunction among Type 2 Diabetic Patients in Saudi Arabia showed that 15.3%, of DM patients had clinical hypothyroidism, and 9.5% had subclinical hypothyroidism[19].

Another study done by ***Perros et al*** [20], studied a randomly selected group of 1310 diabetic adults and found the overall prevalence of thyroid disease to be 13.4%. ***Smithson*** [21] reported a prevalence of undiagnosed thyroid disease in 5.5% of diabetics receiving community diabetes care while the prevalence in the entire population of diabetic patients registered in general practice was 10.8%.

When comparing hypothyroidism with type 1 DM (T1DM) versus T2DM, the former was significantly associated with hypothyroidism **(P value= 0.013),** consistent with the known increased prevalence of autoimmune conditions in hypothyroid patients. There is increased prevalence of thyroid disease in T2DM, but it has a lower prevalence compared to T1DM [22].Several studies have shown the association between thyroid autoimmunity and type 1 diabetes [23, 24]. Our findings are in agreement with what has been reported. ***Smithson*** [21]supports the theory that the high prevalence of abnormal thyroid function tests might result from the prevalence of thyroid antibodies in patients with DM and the influence of poorly controlled diabetes on thyroid hormone concentrations. Others support the idea that hypothyroidism and DM have autoimmune features[25].

Marital status has a statistically significant value in comparison with hypothyroidism (P value= 0.0001). Married subjects were more prone to hypothyroidism than non-married, which could be explained by the increased physiological needs of pregnancy and lactation.

Hypothyroidism patients usually have a higher BMI [26, 27] but in our study we didn't find any significant difference between the BMI groups and hypothyroidism, however most of our subjects (57.4%) were either overweight or obese. We found that Rh blood type, educational level, working status and hypertension had no statistically significant association with hypothyroidism. We have found that female gender and diabetes are significant risk factors for hypothyroidism.

CONCLUSION AND RECOMMENDATIONS:

Our findings support the need for further investigation to look for the association between ABO blood groups and hypothyroidism, further investigations in a larger population are warranted. Future advances in molecular biologic techniques, immunology, and human genetics combined with rigorous epidemiological assessments should clarify our observations.

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