DIAGNOSTIC VALUE OF JAK2 V617F MUTATIONAL SCREENING IN PATIENTS WITH BUDD-CHIARI SYNDROME

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ABSTRACT:

Background: *The diagnosis of underlying myeloproliferative neoplasms (MPNs) is often problematic in patients with Budd Chiari syndrome (BCS). A clonal mutation in JAK2 tyrosine kinase (JAK2V617F) occurs in a high proportion of patients with MPNs and is of use in the characterization of occult MPNs in BCS.*

Aim of the work: *Detection of JAK2 V617F mutation in patients with BCS and its value in detection of occult MPNs.*

Patients and Methods: *This study was carried out on fifty seven newly diagnosed Budd Chiari syndrome patientswho were attending tropical department in Ain Shams University Hospitals during the period from July 2017 to July 2018.Detection of JAK2V617F mutation was done by real time polymerase chain reaction.*

Results: *Out of the studied 57 BCS patients, JAK2 V617F mutation was detected in 12 patients (21.1%) {10 (83.3%) were heterozygous and 2(16.7%) were homozygous for mutation}, while 45 patients (78.9%) were negative.On comparing JAK2 V617F positive and negative groups, there was a highly statistically significant relation regarding MPNs diagnosis, where all JAK2 V617F positive patients were diagnosed as MPNs of whom 7 (58.3%) had overt presentation and 5(41.7%) had occult presentation, while in JAK2 V617F negative patients only 2 were diagnosed overt MPNs (p=0.001).*

Conclusion: *In conclusion the JAK2 V617F mutation is an acquired mutation that can be used for diagnosis of latent MPNs presenting with thrombotic events, thus it is recommended to include JAK2 V617F gene analysis in the research panel for BCS patients.*

Keywords: *JAK2 V617Fmutation, Budd Chiari Syndrome, Real Time PCR, Myeloproliferative Neoplasms.*

INTRODUCTION

Budd-Chiari syndrome is a life-threatening group of disorders that result from obstruction of hepatic venous outflow, that may occur at the level of the hepatic venules (hepatic veno-occlusive disease), the large hepatic veins, inferior vena cava (IVC), or the right atrium (congestive hepatopathy)[1]. BCSare relatively rare disorders; however, can be fatal if the underlying etiological factors are not diagnosed and treated [2].

Etiological factors in a significant proportion of BCS cases include: thrombo-philic abnormalities and clonal disorders of hematopoiesis, such as Philadelphia chromosome negative myeloproliferative neoplasms both overt and occult [2].The distinction between these two pathogenic mechanisms may have important clinical

implications due to different treatment modalities [3].

The diagnosis of MPNs in patients with BCS is often difficult at the time of acute thrombosis, as well as during the post thrombotic period. Some factors e.g. hemodilution, occult bleeding, and hypersplenism due to portal hypertension may obscure changes in blood cell counts used for diagnosing MPNs [4].

Janus kinase 2 (JAK2) is a cytoplasmic tyrosine kinase that transduces signals triggered by hematopoietic growth factors such as erythropoietin in normal and neoplastic cells. The acquired gene mutation on chromosome 9 (JAK2 V617F) is associated with polycythemia vera and other related MPNs [2]

JAK2 V617F-positive MPNs are one of the most frequent thrombotic conditions underlying a diagnosis of BCS [5].Therefore, to screen for JAK2 V617F mutation in patients with BCS is considered a valuable method for diagnosing occult MPNs presenting with thrombotic events[2]

AIM OF THE WORK:

This study aims at detection of JAK2 V617F mutation in patients with BCS and its value in detection of occult MPNs.

SUBJECTS AND METHODS:

Study Subjects:

The present study was carried out on fifty seven newly diagnosed Budd Chiari syndrome patients who were attending tropical department in Ain Shams University Hospitals during the period from July 2017 to July 2018. Verbal informed consent was obtained from all patients.

- **To reach diagnosis and classification, all patients were subjected to the following:**

A. **Complete history taking** stressing on transient risk factors for venous thromboembolism (including surgery, pregnancy, puerperium, oral contraceptive use, hormone replacement therapy, trauma, malignancy, prolonged immobilization (>10 days), and extensive travel (>8 hours) in addition to thorough clinical examination.

B. **Color Doppler ultrasound** for the evaluation of the IVC, and hepatic vein.

C. **Laboratory investigations** which include:

- Complete blood picture using Coulter LH 750 analyzer (coulter electronics, Hialeah, FL, USA).
- Prothrombin time (PT), INR and activated partial thromboplastin time (APTT) using Stago Compact analyzer (Germany).
- Thrombophilia screening tests: prothrombin G20210A mutation, methyl tetrahydrofolatereductase (MTHFR) mutation, Factor V Leiden mutation, serum level of antithrombin, protein C, protein S, and antiphospholipid antibodies (lupus anticoagulant and anticardiolipin). The screening tests results were obtained from patient files.
- Investigations for presence of any associated Philadelphia negative MPNs according to WHO 2016 diagnostic criteria[6]
- Detection of JAK2V617F mutation by real time polymerase chain reaction (RT-PCR) using Slan 96P real time PCR system (SANSURE BIOTECH INC, China) using ipsogen JAK2 Muta Screen Kit (catalog no. 673022).

Methods:

Detection JAK2V617F mutation by (real time PCR): all samples were analysed for JAK2V617F mutation by real time polymerase chain reaction) using Slan 96P Real Time PCR System (SANSURE BIOTECH INC, China) using ipsogen JAK2

Muta Screen Kitafter DNA extractionfrom fresh PB samples with QIAampDNA mini kit (Qiagen, Germany) according to manufacturer's spin protocol.

Statistical analysis:

All data were analyzed using SPSS Version 20.0. (Armonk, NY: IBM Corp). Data are expressed as mean± standard deviation (SD) or frequency and percentage as appropriate. Differences in discrete variables between groups were evaluated using the chi-square, student t or fishers exact tests according to sample size.

RESULTS

Demographic and Clinical data (Table 1):

Out of 57 BCS patients; 23(40.4%) were males and 34(59.6%) were females with male to female ratio 1: 1.4. Their ages ranged from 13 to 55 with mean of 27.9 ±8 years. One (1.8%) patient presented with isolated splenomegaly, 12 (21.1%) with isolated hepatomegaly, while 36 (63.2%) with combined hepatosplenomegaly. Seven (12.3%) had history of thrombosis at sites other than hepatic veins and 9 (15.8%) had history of oral/ genital ulcers.According to clinical presentation; 36 (63.2%) had chronic onset while 11 (19.3%) and 10 (17.5%) had sub-acute and acute onset respectively.

Table (1): Description of demographic and clinical data

Parameter		Range [(Mean ± SD)
Age (years)		13-55(27.91±8.13)
Parameter		Number (%)
Sex	Male	23 (40.4%)
	Female	34(59.6%)
	Male:Female ratio	1: 1.4
Organomegaly	Hepatomegaly	12 (21.1%)
	Splenomegaly	1 (1.8%)
	Hepatosplenomegaly	36 (63.1%)
History	Thrombosis in other sites	7(12.3%)
	Oral/Genital ulcer	9(15.8%)
Clinical presentation	Acute	10(17.5%)
	Sub-acute	11(19.3%)
	Chronic	36(63.2%)

SD: standard deviation.

Laboratory and Radiological data (Table 2)

Regarding laboratory data, complete blood picture (CBC) parameters showed hemoglobin concentration ranged from (7-17) g/dL with mean value of 12.24 ± 2.40 g/dL, total leucocytic count ranged from (1.60-26) $x10^9$/L with median of 7.3(IQR: 5-10.9)$x10^9$/L and the platelet count ranged from (37-909) x 10^9/L with mean value of 234.60 ± 189.52$x10^9$/L.

Coagulation profile showed PT ranged from 11-34 seconds with mean value of 14.36 ± 3.84, INR ranged from 0.90-2.50 with mean value of 1.28 ± 0.34 and APTT ranged from 26-65 seconds with mean value of 30.49 ± 8.68.

Concerning the site of thrombosis; 48 (84.2%) had MHV thrombosis, 52(91.2%) had LHV thrombosis and 50(87.7%) had RHV thrombosis, while 9 (15.8%) had associated IVC thrombosis and 2 (3.5%) had associated PV thrombosis.

Table (2): Description of site of thrombosis and laboratory data

Parameter		**Range [(Mean ± SD) or (Median IQR)*]**
CBC parmeters	Hb (g/dL)	7- 17(12.24±2.4)
	TLC ($x10^9$/L)	1.6- 26[7.3(5-10.9) *]
	Platelets ($x10^9$/L)	37-909 (234.6±189.52)
Coagulation profile	PT (seconds)	11- 34(14.36±3.84)
	INR	0.90-2.50(1.28±0.34)
	APTT (seconds)	26-65(30.49±8.68)
Location of thrombosis by doppler Ultra sound	MHV thrombosis	48(84.2%)
	RHV thrombosis	50(87.7%)
	L HV thrombosis	52(91.2%)
	PV thrombosis	2(3.5%)
	IVC thrombosis	9(15.8%)

SD: standard deviation, IQR: inter quartile range, CBC: complete blood picture, Hb: hemoglobin, TLC: total leucocytic count, PT: prothrombin time, INR: international normalized ratio, APTT: activated partial thromboblastin time, MHV: main hepatic vein, RHV: righ hepatic vein, LHV: left hepatic vein, PV: portal vein, IVC: inferior vena cava.

Etiological factors of Budd Chiari Syndrome (Table 3)

The studied patients were divided according to the etiology of intravascular thrombosis into two groups; 19/57(33.3%) of idiopathic etiology (no evident secondary pro-thrombotic factor for thrombosis) and 38/57 (66.7%) secondary to other pro-thrombotic factors. Secondary pro-thrombotic factors were found either single factor in 17/38 (44.7%) or a combination of multiple secondary prothrombotic factors in 21/38 (55.3%) of patient.

The most common secondary pro-thrombotic factor was methyl tetra hydropholatere- ductase (MTHFR) mutation, detected in 24 patients (42.1%) {23 (95.8%) were heterozygous and 1(4.2%) was homozygous for mutation} followed by factor V Lieden mutation detected in 17 (29.8%) patients {14 (82.4%) were heterozygous and 3(17.6%) were homozygous for mutation}, followed by MPNs diagnosed in 14 (24.6%) patients; of whom 5 (8.8 %) were diagnosed as occult MPNs and 9(15.8%) were diagnosed as overt MPNs (PV=5, ET=4). Other secondary pro-thrombotic factors include Behcet disease which was diagnosed in 10 (17.9%) patients, antiphospholipid syndrome was diagnosed in 8 (14%) patients, pregnancy was found in 7 (12.3%) patients, hormonal replacement therapy was taken in 5 (8.8%) patients, protein C deficiency was found in 3 (5.3%) patients, prothrombin G 20210A mutation detected in 2 (3.5%) patients, while protein S deficiency was found in only one (1.8%) patient. None of our patients had anti thrombin III deficiency or PNH.

Table (3): Description of Etiological factors of Budd Chiari Syndrome

Parameter			Number (%)
Etiology	Idiopathic		19(33.3%)
	Secondary causes		38(66.7%)
		Single factor	17 (44.7%)
		Combined faactors	21 (55.3%)
	MTHFR mutation		24(42.1%)
	Type of MTHFR Mutation	Homozygous	1 (2.5%)
		Heterozygous	23(95.5%)
	FVL mutation		17(29.8%)
	Type of FVL mutation	Homo	3(17.6%)
		Hetero	14(82.4%)
	MPNs		14(24.6%)
		Overt	9(15.8%)
		Occult	5(8.8%)
	Behcet disease		10(17.9%)
	Antiphospholipid antibody syndrome		8(14%)
		AnticardiolipinIg M	4 (7%)
		Lupus anticoagulant	7 (12.3%)
	Pregnancy		7(12.3%)
	Hormonal therapy		5(8.8%)
	Protein C deficiency		3(%5.3)
	Prothrombin G 20210A mutation (Heterozygous)		2(3.5%)
	Protein S deficiency		1(1.8%)

MPNs: myeloproliferative neoplasms, MTHFR: methyl tetrahydropholatereductase, FVL: factor v Leiden.

JAK2 V617F mutational status in relation to etiology of BCS (Table 4)

Out of 12 JAK2 V617F positive patients, 4 (33.3%)had idiopathic etiology and 8 (66.7%) patients had associated secondary pro-thrombotic factors while the 45 JAK2V617F negative patients 15(33.3%) had idiopathic etiology and 30(66.7%) had associated secondary pro-thrombotic factors.

Table (4): Comparison between negative and positive JAK2 V617F mutation cases as regard etiology of BCS

	JAK2 V617F Positive (n=12) Number (%)	JAK2 V617F Negative (n=45) Number (%)
Idiopathic cases (n=19)	4 (33.3%)	15 (33.3%)
Secondary cases (n=38)	8 (66.7%)	30 (66.7%)

JAK2 V617F: janus kinase 2 V617F

JAK2 V617F mutational status in relation to secondary pro-thrombotic factors (Table 5)

On comparing JAK2 V617F positive and negative groups, there was a highly statistically significant relation regarding MPNs diagnosis, where all JAK2 V617F positive patients were diagnosed as MPNs of whom 7 (58.3%) had overt presentation and 5(41.7%) had occult presentation, while in JAK2 V617F negative patients only 2 were diagnosed overt MPNs (p=0.001). No significant association was found on comparing both groups regarding other secondary pro-thrombotic factors**.**

Table (5): Comparison between negative and positive JAK2 V617F mutation cases as regard secondary pro-thrombotic factors

Parameter			JAK2 V617F positive (n=12) Number (%)	JAK2 V617F negative (n=45) (Number (%)	P Value	Sig
Secondary Causes	Protein C deficiency		1(8.3%)	2(4.4%)	0.51**	NS
	Protein S deficiency		0(0.0%)	1(2.2%)	1.0**	NS
	MPNs		12(100%)	2(4.4%)	0.001**	HS
	Type of MPNs	Overt	7(58.3)	2(4.4%)		
		Occult	5(41.7)	0(0%)		
	FVL mutation		2(%16.7)	15(33.3%)	0.31**	NS
	Prothrombin G 20210A mutation		0(0%)	2(4.4%)	1.0	NS
	MTHFR mutation		4(33.3%)	20(44.4%)	0.489*	NS
	Antiphospholipid antibody syndrome		2(16.7%)	6(13.3%)	0.670**	NS
	Behcet disease		2(16.7%)	8(18.2%)	1.0**	NS
	Hormonal therapy		1(8.3%)	4(8.9%)	1.0**	NS
	Pregnancy		7(15.6%)	0(0.0%)	0.32**	NS

JAK2 V617F: janus kinase 2 V617F, MPNs: myeloproliferative neoplasms, MTHFR: methyl tetrahydropholatereductase, FVL: factor v leiden, NS: non-significant, HS highly significant, *Student t test, **Fisher exact test, sig: significance

Occult versus overt MPNs cases (Table 6)

MPNs were diagnosed in 14 patients (24.6%); of whom 5 (8.8 %) were diagnosed as occult MPNs and 9(15.8%) were diagnosed as overt MPNs (PV=5, ET=4). All occult MPNs patients showed JAK2 V617F mutation 5(100%), while in overt MPNs patients, JAK2 V617F mutation was detected in 7(77.8%) and the remaining 2 patients (22.2%) had wild type JAK2 V617F (the diagnosis depended on other WHO 2016 criteria For PV and ET).

As regard CBC parameters, mean hemoglobin, TLC and platelets were higher in overt cases than occult cases, and overt cases are more associated with secondary pro-thrombotic risk factors.

Table (6):Comparison between occult and overt MPNs

		overt cases (n=9) (Mean ± SD)	Occult cases (n=5) (Mean ± SD)
Age (years)		27.4± 7.1	32.4 ± 9.2
Parameter		Number (%)	Number (%)
Sex	Male	5(55.5%)	2(40%)
	Female	4(44.4%)	3(60%)
	M: F ratio	1.2:1	1:1.5
Parameter		(Mean ± SD)	(Mean ± SD)
CBC parameters	Hb (g/dl)	14.6± 2.5	11.42 ± 2.3
	TLC ($x10^9$/L)	12.1 ± 6.3	6.76 ± 1.9
	Platelets ($x10^9$/L)	545.6 ± 266.9	115.4 ± 65.3
Coagulation profile	PT (seconds)	14.6 ± 3.9	12 ± 0.7
	INR	1.3 ± 0.4	1.08 ± 0.1
	PTT (seconds)	32.9 ± 12.7	29.6 ± 3.8
Parameter		Number (%)	Number (%)
Etiology	Isolated	3(33.3%)	4(80%)

	MPNs		
	Associated secondary cause	6 (66.7%)	1 (20%)
JAK2 V617F Mutation	Positive	7 (77.8%)	5 (100%)

SD: standard deviation, CBC: complete blood picture, Hb: hemoglobin, TLC: total leucocytic count, PT: prothrombin time, INR: international normalized ratio, APTT: activated partial thromboblastintime, JAK2 V617F: janus kinase 2 V617F, MPNs: myeloproliferative neoplasms.

DISCUSSION:

Budd-chiari syndrome is a hepatic venous outflow tract obstruction. It could be primary from vein thrombosis or secondary from a compression or invasion of the vein as in malignancy **[7].**

Thrombophilia abnormalities and clonal disorders of hematopoiesis such as Philadelphia chromosome negative MPNs are the two main mechanisms of intravascular thrombosis in a significant proportion of BCS. According to *EL Sebay et al.,*[8] BCS patients with MPN carry significant poorer prognostic features that need earlier hepatic decompression procedure.

Moreover the distinction between these two pathogenic mechanisms has important clinical implications because anticoagulants are the most rational treatment in cases of thrombophilia, whereas cytoreductive therapy is indicated in patients with MPNs **[2]**

The diagnosis of thrombophilia is relatively simple and accurate but the diagnosis of MPNs is often problematic in patients with BCS as hemodilution, occult bleeding, and hypersplenism due to portal hypertension may mask changes in blood cell counts used for diagnosing MPNs**[9].**

Despite suggestive features of MPN in bone marrow, these patients lack adequate diagnostic criteria and are classified as occult MPNs **[10].**

According to *Karaköse et al.,*[2]overt MPNs are observed in 23%-31.2% of patients with BCS which increases to 45%-53% when occult MPNs are included as an etiological factor.

In 2016 *El Sebay and colleages* suggested that testing JAK2 V617F should replace bone marrow examination as initial test for MPNs in BCS patients.Thus the aim of this work was to detect JAK2V617F mutation in patients with BCS and determine its value in detection of occult MPNs.

Our study involved 57 BCS patients divided according to the etiology of intravascular thrombosis into 2 groups, 19/57 (33.3%) of idiopathic etiology and 38/57(66.7%) secondary to other pro-thrombotic factors.

In the present study JAK2 V617F mutation was positive in 12/57 (21.1%) of the studied patients of whom 83.3% (10/12) were heterozygous and 16.7% (2/12) were homozygous for mutation. This is consistent with ***Helman et al.,*** **[5]** who identified JAK2 V617F mutation in 10/32 (31.2%) of BCS patients and ***Sakr et al.,*** **[11]** who identified JAK2 V617F mutation in 18/62(29%) of BCS patients.

However in a study done by *El Sebay et al.,*[12], the frequency of JAK2 V617F mutation was lower as they identified 4/35 (11.4%) of BCS patients all of them were of heterozygous for mutation. This difference may be attributed to using different method

of detection (polymerase chain reaction-restriction fragment length polymorphism).

Also lower frequencies of JAK2 V617F mutation were reported by 2 different studies done by Chinese authors*Wang et al.,* [13]and*Qi et al.,* [14]whoidentifiedJAK2 V617F mutation in 2.37% (7/295) and in4.3% (4/92) respectively. Accordingly *Wang et al.,* [13] stated that MPNs were uncommon risk factor for BCS in china.

In our study, JAK2V617F mutation was positive in 5/19(26.3%) of idiopathic BCS patients and in 7/37(18.4%) of secondary BCS patients. The idiopathic JAK2V617F positive patients were not diagnosed as overt MPNs (not fulfilling WHO 2016 diagnostic criteria), and could be considered as occult MPNs. Similarly, *De Stefano et al.,* [15] reported JAK2V617F mutation in 33.3% of idiopathic BCS patients. Also, *Karaköse et al.,* [2]found the frequency ofJAK2 V617F mutation in 21.4 % of patients with idiopathic BCS (all were considered occult MPNs) and in 17.6% of patients with secondary pro-thrombotic factors.

In our study, on comparing JAK2 V617F positive and negative patients, there was no statistically significant difference regarding associated inherited or acquired pro-thrombotic risk factors except for MPNs. The same was reported by *Colaizzo et al.,* [16]. However, *Karaköse et al.,* [2] reported additional pro-thrombotic factor that showed statistically significant association (FVL mutation), and this is in agreement with*Denninger et al.,* [17] who stated that the role of multiple factors in the etiology of thrombosis should not be ignored

In our study out of 12 JAK2V617F positive BCS patients, 5(41.7%) had occult presentation for MPNs and 7(58.3%) had overt presentation However *Yonal et al.*,[18] identified out of 8 JAK2 V617F positive BCS patients 2 (25%) with overt MPNs and 6(75%) with occult presentation for MPNs. Also Sakr et al., [11] identified out of 18 JAK2 V617F positive BCS patients, 28.5% and 71.5% with overt and occult presentation for MPNS respectively.

In the current study, overt MPNs were diagnosed in 9 (15.8%) patients of whom 7 (77%) had JAK2 V617 mutation, and occult MPNs were diagnosed in 5 (8.8 %) patients, all of them (100%) had JAK2 V617 mutation. Similarly, a study done by *Karaköse et al.,* [2] reported that overt MPNs were diagnosed in 8/111(7.2%) patients, 4 of them had JAK2 V617F mutation and occult MPNs were diagnosed in 6/111(5.4%) patients, all of them had JAK2 V617F mutation. This is also in agreement with *Yonal et al.,* [18]whoidentified overt MPNs in 3/19(15.8%) of BCS patients (2 of them were positive for JAK2 V617F mutation) and occult MPNs in 6/19 (31.6%) all of them were positive for JAK2 V617F mutation.

Also, in our study overt cases showed mean hemoglobin, TLC and platelets higher than occult cases and this prove that hematological parameters are not reliable for diagnosis of occult MPNs

These results substantiate inclusion of JAK2V617F in the routine diagnostic work up of BCS patients regardless the absence of MPN hallmarks such as elevated peripheral blood count, as screening for the JAK2 V617 mutation is a valuable method for diagnosing occult MPNs.

Conclusion:

JAK2 V617F mutation is an acquired mutation used for the diagnosis of occult MPNs presenting with thrombotic events. Analysis of JAK2 mutations JAK2 gene analysis should be included in the research panel for BCS patients.

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القيمه التشخيصيه لفحص طفره جانوس كيناز2 V617F في المرضى الذين يعانون من متلازمة بود كيارى

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القسم : الباثولوجيا الاكلنيكيه - كلية الطب جامعة عين شمس

مقدمه: إن إضطرابات نمو النخاغ مثل أورام التكاثر الإبيضاضى مع فيلادلفيا سلبية ، هي من العوامل المسببة لنسبة كبيرة من حالات متلازمة بود كيارى. و تشخيص أورام التكاثر الإبيضاضى في المرضى الذين يعانون من متلازمة بود كيارى غالبا ما يكون إشكالية. وتعتبر أورام التكاثر الإبيضاضى مع وجود نتيجه ايجابيه لفحص طفره JAK2V617F هي واحدة من الحالات الأكثر شيوعا للجلطات الكامنة وراء تشخيص متلازمه بود كيارى

الهدف من الدراسه: تهدف هذه الدراسة للكشف عن طفرة جانوس كيناز 2V617F في المرضى الذين يعانون من متلازمه بود كيارى وقيمته في الكشف عن حالات أورام التكاثر الإبيضاضى الغامض

المرضي و طرق البحث: تم اجراء هذه الدراسة على مرضى متلازمة بود كيارى حديثي التشخيص المتوافدين علي مستشفيات جامعة عين شمس فى الفتره من يوليو ٢٠١٧ الى سبتمبر ٢٠١٨ . وقد تم الكشف عن طفرة جانوس كيناز2V617Fبواسطة تفاعل البوليميريز المتسلسل.

النتائج: وقد تم اكتشاف طفرة JAK2 V617F في ١٢ مريضا (٢١.١ ٪) {١٠ (٨٣.٣ ٪) كانوا مختلفان للطفره و ٢ (١٦.٧ ٪) متماثلان للطفرة } ، في حين أن ٤٥ مريضا (٧٨.٩ ٪) كانت نتاءجهم سلبية. عند مقارنة المجموعات الإيجابية والسلبية لـ طفره جانوس كيناز٢ V617F ، كانت هناك علاقة ذات دلالة إحصائية عالية فيما يتعلق بتشخيص أورام التكاثر الإبيضاضى ، حيث تم تشخيص جميع المرضى وجود الذين لديهم نتيجه ايجابيه لفحص طفره JAK2V617F على أنهم أورام التكاثر الإبيضاضى منهم ٧ لديهم اعراض واضحه (طبقا لمعايير تشخيص منظمة الصحة العالمية ٢٠١٦) و ٥ كان لديهم اعراض غامضه، في حين تم تشخيص أورام التكاثر الإبيضاضى فى ٢ فقط من المرضى الذين ليهم نتيجه سلبيه للطفره و لم يتم العثور على ارتباط كبيرعند مقارنة كلا المجموعتين فيما يتعلق بالعواملالأخرى.

الملخص: يمكننا أن نستنتج أن طفرة JAK2 V617F هي طفرة مكتسبة ترتبط مع أورام التكاثر الإبيضاضى الخفية التي يمكن استخدامها لتشخيص أورام التكاثر الإبيضاضى الكامنة التي تظهر باعراض التجلط ولذلك يجب ضم تحليل الجينات JAK2 في قائمه الفحوصات للمرضى الذين يعانون من متلازمه البود كيارى.