

Gynecological Aspect of Behcets Disease Patients

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Abstract: Background: Behcets disease is a systemic inflammatory disease involving many systemic lesions . Aims of the work: To evaluate the gynecological involvement in behcets disease patient. Methods: 30 female patients with behcets disease were evaluated clinically for the prevalence of gynecological ulcer. All of them were subjected to questionnaire including duration of behcets. Result: 86.6% of female patients have a genital ulcer the most common site involved is labia majora Conclusion: gynecological involvement mostly affected female with behcets disease

Keywords: behcets disease genital ulcer .family history

1. Introduction

Behcets disease was first defined by hulusi behcet, a trukish professor of dermatology in 1937 as a tried of recurrent aphthous stomatitis, genital ulceration and relapsing uveitis (Behcet 1937).

Behcets disease considering as a chronic relapsing multisystemic inflammatory disease with unpredictable exacerbation and remission process with a clinical features of mucocutaneous lesions ,and ocular ,vascular,reticular ,gastrointestinal, neurological ,urogenital ,pulmonary ,and cardiac involvement (SakaneT .et al,1999)

The etiopathogenesis of disease remains unknown, although several immunological abnormalities have been demonstrated in patients with behcets disease, the exact mechanism of the inflammatory changes occurring also remains to be elucidated.(Erkanalpsoy. et al,1998)

Genital ulcers are the second main symptoms encountered , the lesion are present in varying proportions , ranging from 57 to 93%(zouboulis et.al, 1999. et al 1997, chatejv. et al, 199) they are similar in appearance and course to oral ulcer but may not recur as often and have scarring tendency .

Genital ulcer are usually deeper than the oral ulcer and their appearance can be preceded by a tender nodule .they are usually painful or accessional a asymptotic (Bang.etal,1997,Chatejv. et al ,1999,Schreiner D 1987,Alposy. et al, 2002)

Genital ulcer may not recur as often as oral ulcer and can have scaring tendency usually oval and or round well demarcated with grayish yellow necrotic base and erythematous rim and the main site are the labia majra ,labia minora ,vulva and perineum(Arbesfeld. et al ,1988,and Golen.etal, 1994)

Several studies was conducted in Iraq regarding behcet syndrome up to our knowledge few of these studies were emphasize of the gynecological aspect, therefore this study was intensively showed the relevance of genital ulceration in female patients with behcets disease

2. Aims of the Study

This study was conducting to

- 1) Evaluate the prevalence of clinical finding of genital ulceration in behcets disease
- 2) Correlate the clinical finding with the age ,age of onset ,age of presentation ,a familiar medical history ,the result of the traditional pathergy test , site and the number of the genital ulcer ,evidence of scarring and pain associated symptoms

3. Materials and Methods

Thirty female patients were involved this study attended to gynecological clinic they were referred from dermatological clinic, all patients were Iraqi female aged between 20- 45 years. period (june 2013 to august 2017)

All patients were diagnosed by a specialized dermatologist on basis of international behcets disease criteria reported in 1990.

Inform concerned was clarified to each patients participated in this study with agreement signature from each patient the following were recoded from each patient ;age at presentation and diagnosis, familial medical history and result of traditional pathergy reaction also the site, size of genital ulcer, evidence of scaring and age at onset of a genital ulcer. Pain with genital ulcer was classified according to the visual analogue score .the type of ulcer were classified according to (Senusi.et al ,2015)

- Minor aphthae smaller than 1 cm heal without scar formation
- Major aphthae larger than 1 cm heal with scar
- Herpeti form aphthae are multiple smaller ulcer (pin point)
- The vaginal examination was based on the American criteria 2014

Exclusion criteria

- During menstruation
- Presence of inflammation.
- Presence of bruising and tearing

The labia major was evaluated and the position and symmetry are assessed by a gynecological specialized the examiner was looking for the presence of ulcers, inflammation, warts and rashes

- The labia minora are then evaluated color, texture, presence of ulcer, inflammation, and the presence of tearing
- The clitoris is assessed for size position symmetry and inflammation
- The urthral opening is inspected
- The vaginal opening is inspected for position bruising, warts
- The perineum was inspected
- Pupic area should inspected for any lesion like wart, ulcer, texture

4. Result

This part presents the findings of the data analysis systematically in tables and these correspond with the objectives of this study, and as follows:

4.1 Distribution of studied Parameters

Part 1: Age, Duration, and Free Period of G. Ulcer:

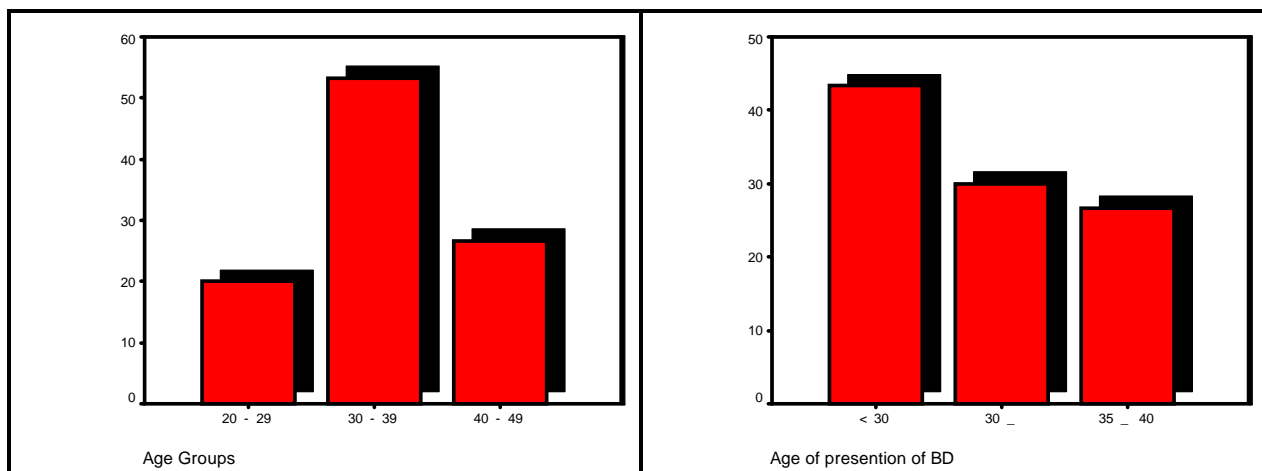
Table (1) shows an observed frequencies, and their percentages for distribution of studied "Age, Duration, and Free Period of G. Ulcer" variables concerning Behcet disease – BD, with comparison's significant.

Table 1: Distribution of Age, Duration, and Free Period of G. Ulcer variables concerning (Behcets Disease) with comparisons significant

Age,Duration, and Free Period of G.Ulcer variables	Classes	No.	%	C.S. (*) P-value
Age Groups Yrs.	20 - 29	6	20	$\chi^2= 5.600$ P=0.061 (NS)
	30 - 39	16	53.3	
	40 - 49	8	26.7	
	Mean \pm SD	34.93 \pm 6.69		
Age at Presentation of BD	< 30	13	43.3	$\chi^2= 1.400$ P=0.497 (NS)
	30 - 34	9	30	
	35 - 40	8	26.7	
	Mean \pm SD	30.63 \pm 5.61		
Age at DX of BD	< 30	6	20	$\chi^2= 7.867$ P=0.049 (S)
	30 - 34	10	33.3	
	35 - 39	12	40	
	Mean \pm SD	33.77 \pm 5.81		
Age at onset of G. Ulcer	20 - 24	3	10	$\chi^2= 7.067$ P=0.070 (NS)
	25 - 29	5	16.7	
	30 - 34	12	40	
	Mean \pm SD	32.20 \pm 5.38		
Duration of G. Ulcer in days	< 5	1	3.3	$\chi^2= 14.600$ P=0.001 (HS)
	5- 9	18	60	
	10- 15	11	36.7	
	Mean \pm SD	8.20 \pm 2.48		
Free period of G.Ulcer in days	< 10	3	10	$\chi^2= 15.800$ P=0.000 (HS)
	10- 14	20	66.7	
	15- 20	7	23.3	
	Mean \pm SD	12.70 \pm 3.43		

(*)HS: Highly Sig. at P<0.01; NS: Non Sig. at P>0.05; Testing based on One-Sample Chi-Square, and Binomial tests.

Figure (1) represented "Age, Duration, and Free Period of G. Ulcer" variables concerning Behcet disease – BD variables.



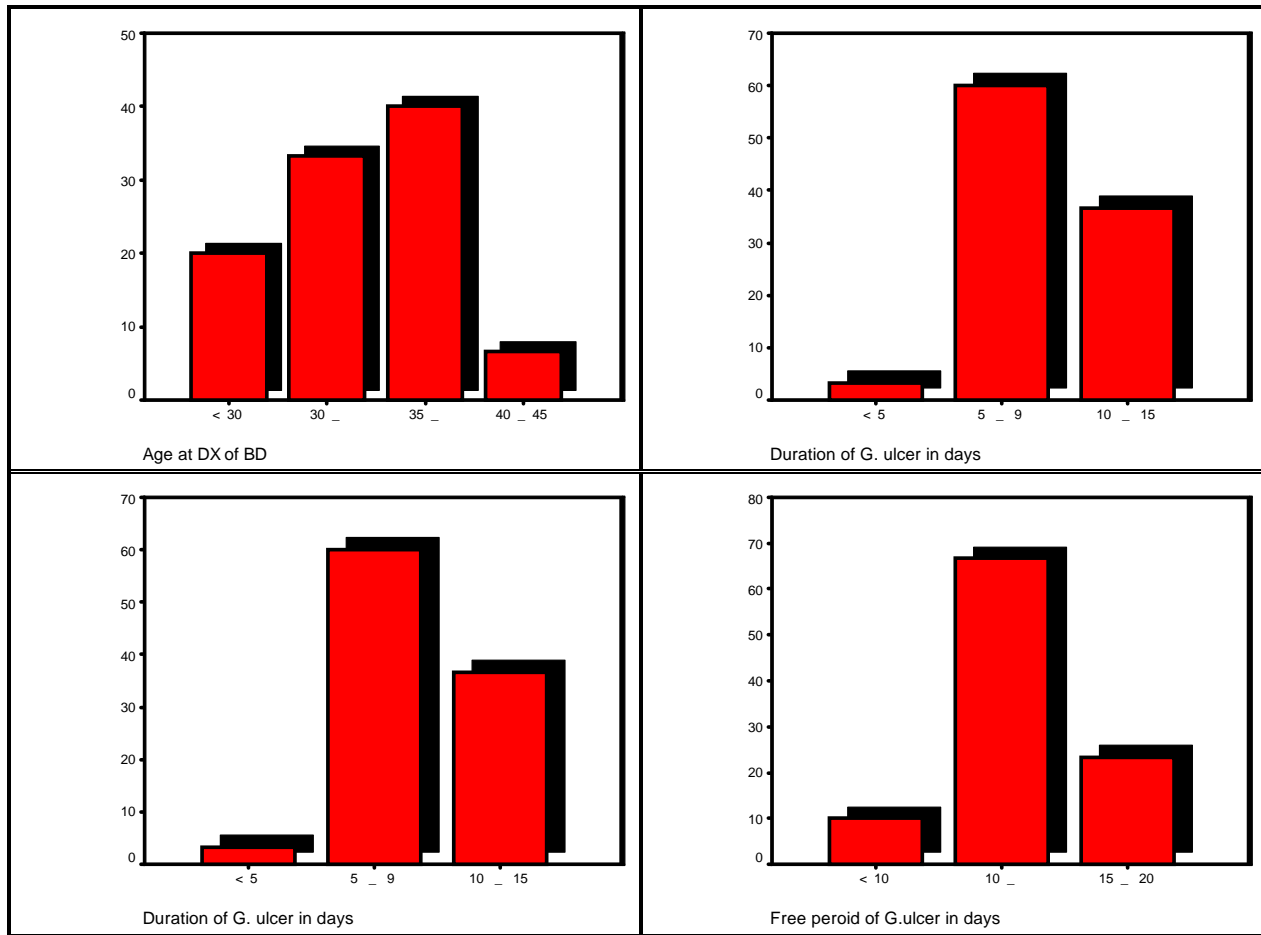


Table 1: Distribution of Age, Duration, and Free period of G. Ulcer variables concerning (Behcet Disease)

Part 2: Risk Factors, Traditional Pathergy test, Symptoms, and Classification):

Table (2) shows an observed frequencies, and their percentages for distribution of studied "Risk Factors, Traditional Pathergy test, Symptoms, and Classification" variables concerning Behcet disease – BD, with comparison's significant.

Table 2: Distribution of Risk Factors, Traditional Pathergy test, Symptoms, and Classification concerning (Behcet Disease) with comparisons significant

Variables	Classes	No	%	C.S. (*) P-value
Family History	Negative	25	83.3	Binomial P=0.001 HS
	Positive	5	16.7	
Traditional Pathergy test	Negative	12	40	Binomial P=0.361 NS
	Positive	18	60	
Oral lesion	Negative	0	0.0	Binomial P=0.000 HS
	Positive	30	100	
Cutaneous lesion	Negative	17	56.7	Binomial P=0.584 NS
	Positive	13	43.3	
G. Ulcer	None	4	13.3	Binomial P=0.000 HS
	Presence	26	86.7	

Site of G. Ulcer	Labia majora	13	43.3	$\chi^2 = 3.800$ P=0.150 (NS)
	Labia minora	12	40	
	Valva	5	16.7	
No. of G. Ulcer	one	27	90	Binomial P=0.001 HS
	two	3	10	
Evidence of Scaring	Negative	23	76.7	Binomial P=0.006 HS
	Positive	7	23.3	
Pain Index	None	6	20	$\chi^2 = 7.400$ P=0.025 (S)
	Sometimes	17	56.7	
	Always	7	23.3	
Classification	Minor	20	66.7	$\chi^2 = 15.800$ P=0.000 (HS)
	Major	7	23.3	
	Herpetiform	3	10	

(*)HS: Highly Sig. at P<0.01; NS: Non Sig. at P>0.05; Testing based on One-Sample Chi-Square, and Binomial tests

Figure (2) represented "Risk Factors, Traditional Pathergy test, Symptoms, and Classification " variables concerning Behcet disease – BD variables.

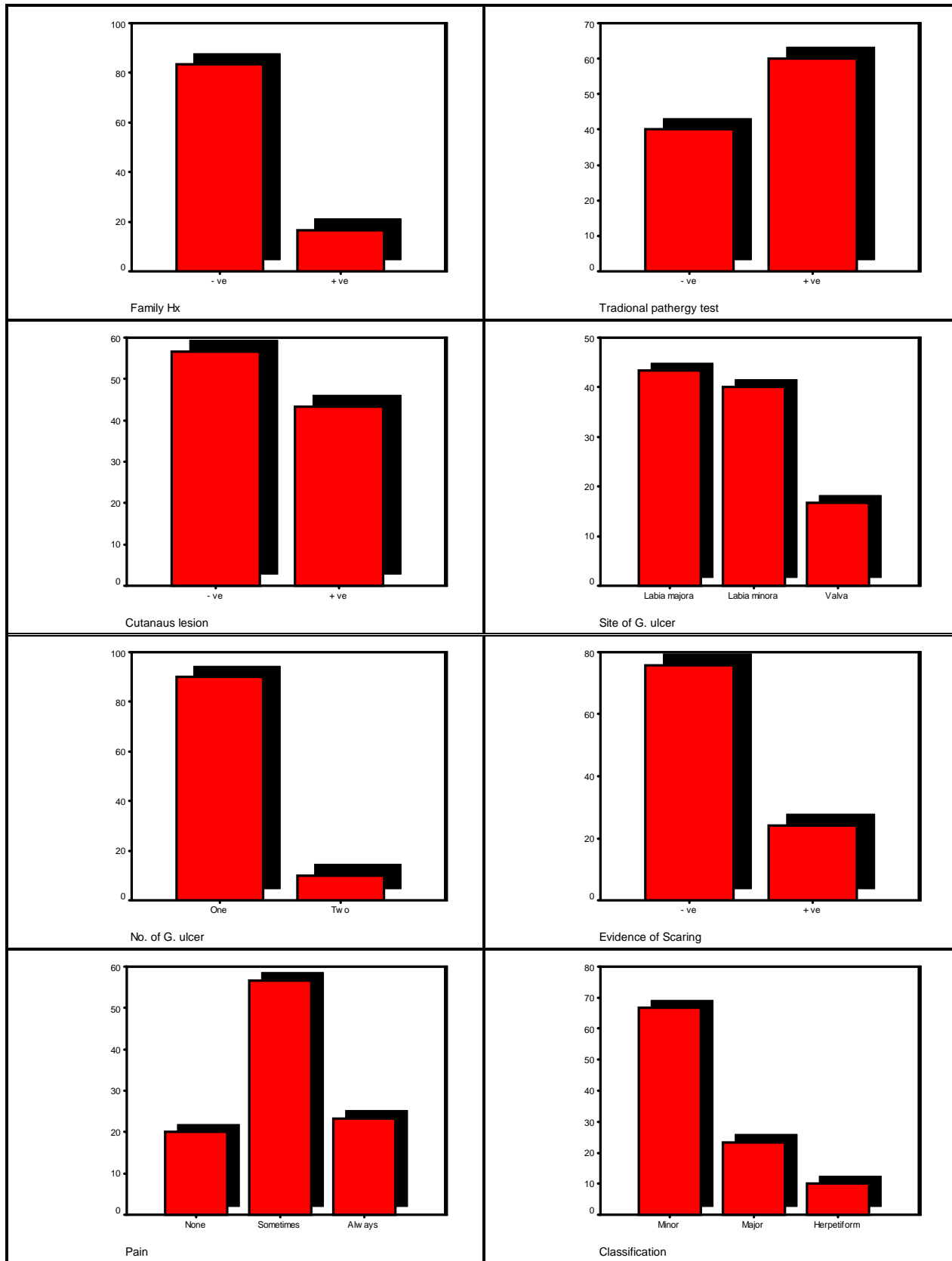


Table 2: Distribution of Risk Factors, Traditional Pathergy test, Symptoms, and Classification concerning (Behcet Disease)

Part 3: Relationships among studied Parameters:

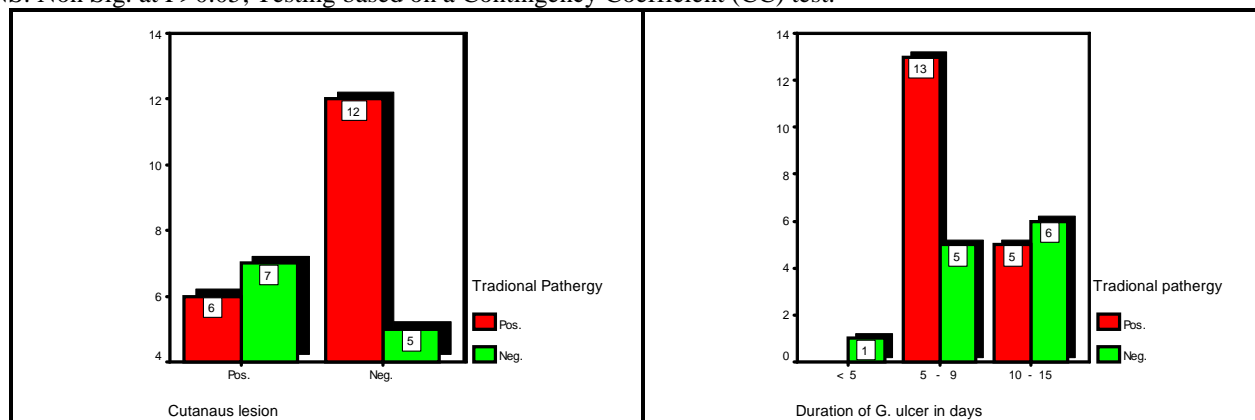
Table (3) shows "Traditional Pathergy test" and studied parameters relationships, as well as Figure (3) illustrated graphically distribution of their observed frequencies.

Table 3: Risk Factors, Symptoms, and Classification distributed according to Traditional Pathergy test outcomes with comparisons significant

Parameters	Response	No. and %	Traditional Pathergy test	Total	C.S. (*)
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			Pos.	Neg.		P-value
Cutaneous lesion	Pos.	No.	6	7	13	CC=0.240 P=0.176 NS
		% T.P. test	33.3%	58.3%	43.3%	
	Neg.	No.	12	5	17	
		% T.P. test	66.7%	41.7%	56.7%	
Duration of G. ulcer in days	< 5	No.	0	1	1	CC=0.327 P=0.166 NS
		% T.P. test	0.00%	8.30%	3.30%	
	5 - 9	No.	13	5	18	
		% T.P. test	72.2%	41.7%	60.0%	
	10 - 15	No.	5	6	11	
		% T.P. test	27.8%	50.0%	36.7%	
Site of G. ulcer	Labia majora	No.	7	6	13	CC=0.259 P=0.339 NS
		% T.P. test	38.90%	50.00%	43.30%	
	Labia minora	No.	9	3	12	
		% T.P. test	50.0%	25.0%	40.0%	
	Valva	No.	2	3	5	
		% T.P. test	11.1%	25.0%	16.7%	
No. of G. ulcer	One	No.	16	11	27	CC=0.045 P=0.804 NS
		% T.P. test	88.9%	91.7%	90.0%	
	Two	No.	2	1	3	
		% T.P. test	11.1%	8.3%	10.0%	
Evidence of Scaring	Pos.	No.	3	4	7	CC=0.190 P=0.290 NS
		% T.P. test	16.7%	33.3%	23.3%	
	Neg.	No.	15	8	23	
		% T.P. test	83.3%	66.7%	76.7%	
Free period of G. ulcer in days	< 10	No.	0	3	3	CC=0.381 P=0.079 NS
		% T.P. test	0.00%	25.00%	10.00%	
	10 - 14	No.	13	7	20	
		% T.P. test	72.2%	58.3%	66.7%	
	15 - 20	No.	5	2	7	
		% T.P. test	27.80%	16.70%	23.30%	
Pain Index	None	No.	4	2	6	CC=0.335 P=0.151 NS
		% T.P. test	22.2%	16.7%	20.0%	
	Sometimes	No.	12	5	17	
		% T.P. test	66.7%	41.7%	56.7%	
	Always	No.	2	5	7	
		% T.P. test	11.1%	41.7%	23.3%	
Classification	Minor	No.	13	7	20	CC=0.190 P=0.571 NS
		% T.P. test	72.2%	58.3%	66.7%	
	Major	No.	3	4	7	
		% T.P. test	16.7%	33.3%	23.3%	
	Herpetiform	No.	2	1	3	
		% T.P. test	11.1%	8.3%	10.0%	

(*) NS: Non Sig. at P>0.05; Testing based on a Contingency Coefficient (CC) test.



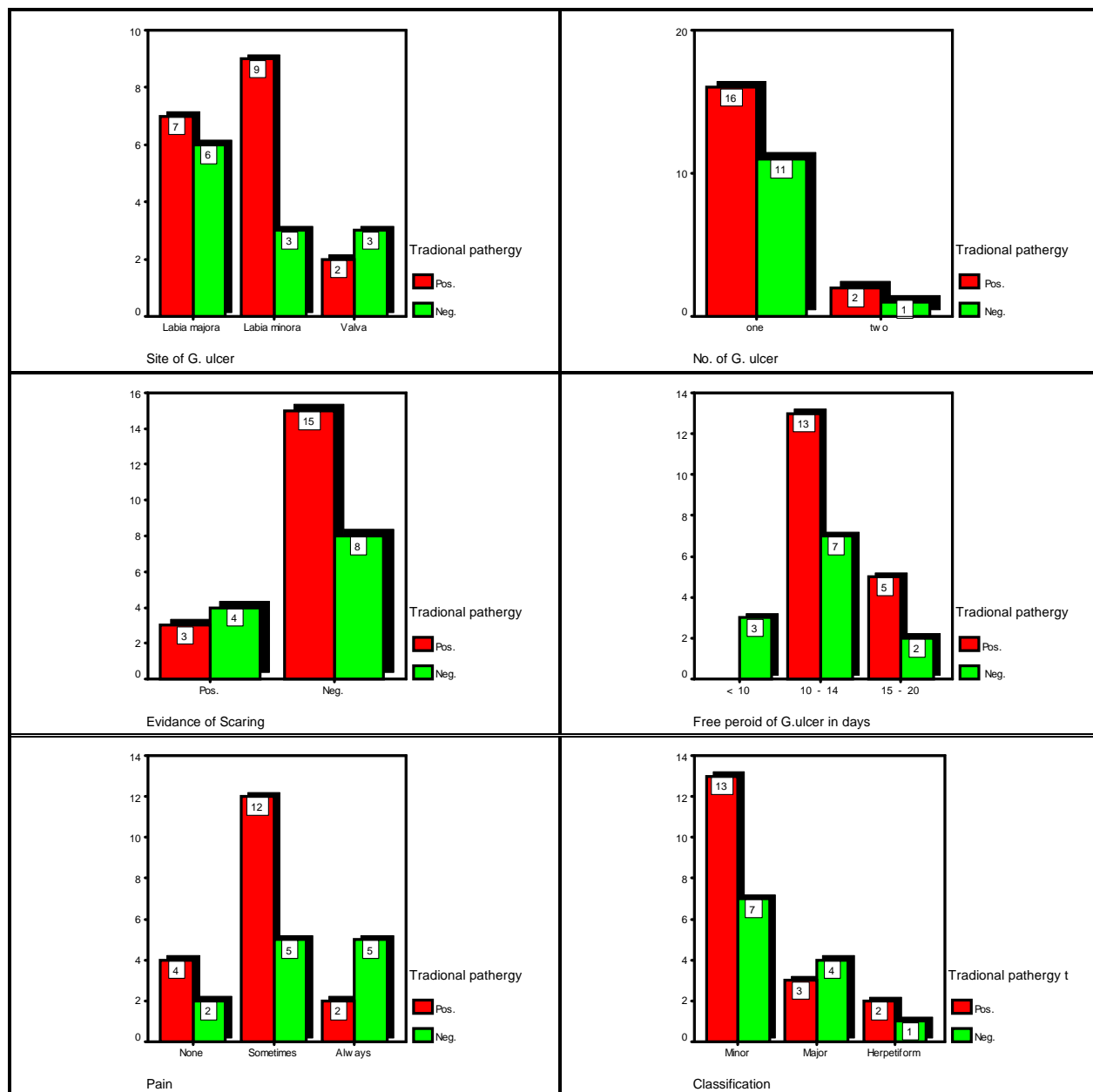


Table 3: Distribution of Risk Factors, Symptoms, and Classification concerning (Behcet Disease) according to Traditional Pathergy test outcomes

Table (4) shows distribution of classification groups and duration of G. ulcer in days relationships, as well as Figure (4) illustrated graphically distribution of their observed frequencies.

Table 4: Distribution (Behcet Disease) Classification according to Duration of G. ulcer in days groups with comparisons significant

Parameter	Groups	No. and %	Classification			Total	C.S. ^(*) P-value
			Minor	Major	Herpetiform		
Duration of G. ulcer in days	< 5	No.	1	0	0	1	CC=0.618 P=0.001 HS
		%	5.0%	0.00%	0.00%	3.3%	
	5 - 9	No.	17	1	0	18	
		%	85.0%	14.3%	0.00%	60.0%	
	10 - 15	No.	2	6	3	11	
		%	10.0%	85.7%	100.0%	36.7%	
	Total	No.	20	7	3	30	
		%	100%	100%	100%	100%	

(*) HS: Highly Sig. at P<0.01; Testing based on Contingency Coefficient test.

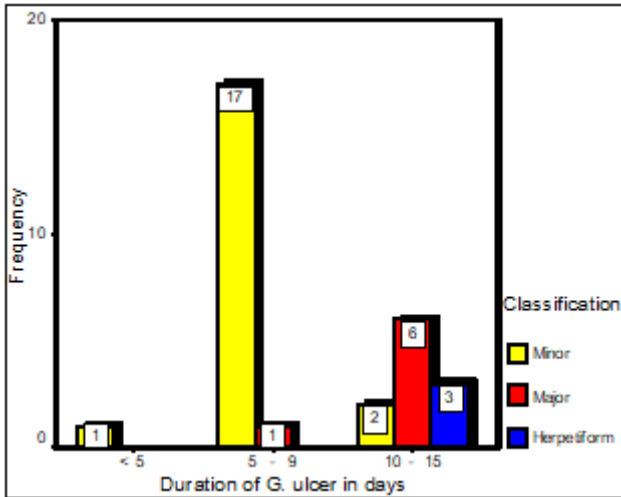


Table 4: Distribution of (Behcet Disease) Classification according to Duration of G. ulcer in days groups

Results show strong relationship are reported amongst distribution of classification groups in contrast of duration of G. ulcer in days, since highly significant different obtained at $P < 0.01$, which indicating that minor level are focusing in second duration's interval, as well as major level are focusing in third duration's interval.

Table (5) shows significant relationship's distribution concerning pain index with studied parameters, as well as Figure (5) illustrated graphically distribution of their observed frequencies.

Table 5: Distribution of Pain responses with significant relationship's Parameters with comparisons significant

Parameter	Response	No. and %	Pain			Total	C.S. ^(*) P-value
			None	Sometimes	Always		
Age of DX of BD	< 30	No.	0	6	0	6	CC=0.546 P=0.048 S
		% Pain	0.00%	35.3%	0.00%	20.0%	
	30 _	No.	3	4	3	10	
		% Pain	50%	23.5%	42.9%	33.3%	
	35 _	No.	3	7	2	12	
		% Pain	50%	41.2%	28.6%	40.0%	
	40 _ 45	No.	0	0	2	2	
		% Pain	0.00%	0.00%	28.6%	6.7%	
Evidence of Scaring	Pos.	No.	0	2	5	7	CC=0.537 P=0.002 HS
		% Pain	0.00%	11.8%	71.4%	23.3%	
	Neg.	No.	6	15	2	23	
		% Pain	100%	88.2%	28.6%	76.7%	
Classification	Minor	No.	6	12	2	20	CC=0.566 P=0.007 HS
		% Pain	100%	70.6%	28.6%	66.7%	
	Major	No.	0	2	5	7	
		% Pain	0.00%	11.8%	71.4%	23.3%	
	Herpetiform	No.	0	3	0	3	
		% Pain	0.00%	17.6%	0.00%	10.0%	

(*) HS: Highly Sig. at $P < 0.01$; S: Sig. at $P < 0.05$; Testing based on Contingency Coefficient test.

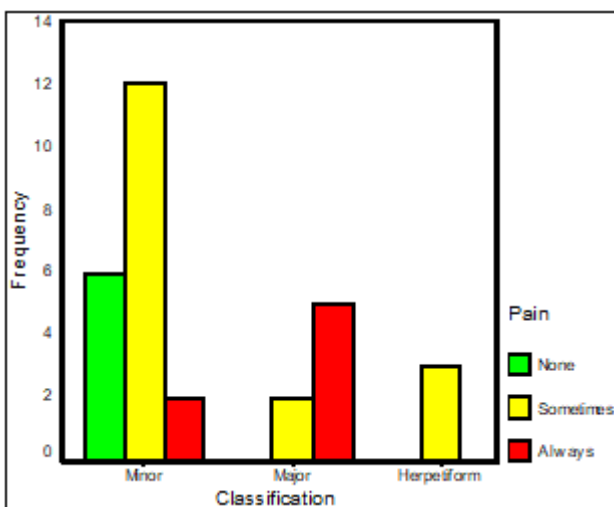


Table 5: Distribution of (Behcet Disease) Classification according to Duration of G. ulcer in days groups

Table (6) shows values of area tests resulted within "Cutaneous lesion", as well as Figure (6) illustrated graphically ROC curve.

Table 6: ROC Curves for "T.P.t." in light of Cutaneous lesion, and Evidence of Scarring Parameters

Test Result Variable: Traditional Pathergy test					
Parameters	Area	Std. Error	Asymptotic Sig.	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
Cutaneous lesion	0.622	0.105	0.258	0.416	0.829
Evidence of Scarring	0.612	0.125	0.377	0.367	0.856

(*) (ROC): Receiver operation characteristic curve
 Non Sig. at $P > 0.05$; The positive actual state is Pos.

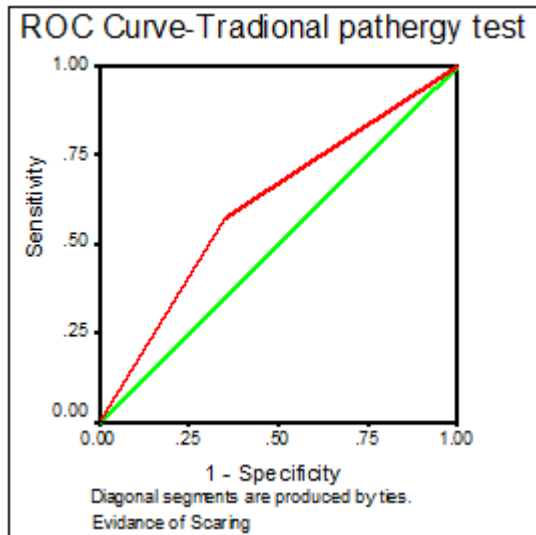


Figure 6: ROC Curves for the for the "Traditional Pathergy test" in light of Cutaneous lesion, and Evidence of Scarring parameters

5. Discussion

Behcets disease is a multisystem disease vasculatities with a high prevalence in turkey ,japan, eastern Mediterrean countries and relatively low in the United state and northen Europe.Usually affects young adult between 20-40 years of age (Mangel . etal ,1996. Aysel, etal .1997, Erkan.et al, 2007 and Virendra. 2014)

Genital ulcer caused by behcets disease are the second most common manifestation of the behcets disease ,occurring in 57% to 96% of the patients (Keoganm. etal, 2009)

However ,Alekbervaz. et al ,2013 found that the two major diagnostic criteria ,namely aphthous stomatitis and the external genital ulcer were found with the same frequency

Although there are many studies of the oral or the other system involvement of BD ,but there are few data on the genital ulcer with evidence of the scar and also the gynecological complaint of these patient ,therefore this study emphasized more on the genital ulcer .

The current study revealed that the mean age was 34.9 year this less than that reported by(Aysel. et al ,1997.Haruko . et al, 2011 .Seyeeh .etal ,2014, Amal. et al, 2015 and Kirino.et al, 2016) ,while almost to be equal to that reported by(Kerkeni.et al, 2010). Regarding age of onset this current study was 30.6 year almost to be equal to that showed by Aysel. et al,1997 and kerkeni. et al, 2010, however the above mentioned could be explain by the ethnic ,regional difference and total sample size .

In current study all of the patient were involved with the oral ulceration however this was disagreed to that showed by (Aysel. et al, 1997.Alaswad 2003, Suna. et al ,2012 and Seyedeh. etal, 2014), they showed that oral ulceration less frequently involved in the patient of the behcets disease but similar that showed by(Ulker. et al, 2007,Kerkeni,et al 2010 and Haruko. et al, 2011)

This is ironically strength the fact that BD diagnostic criteria cannot be confirm unless oral involvement is the initial manifestation

Regarding the cutaneous involvement in BD patients the result of this study showed that half of the patients were involved and that similar to that reported by(Ulker. et al, 2007).on the other hand , ButKerkeni. et al ,2010 ,Haruko.et al ,2011and Seyedeh. et al, 2014 showed a higher percentage of the cutaneous involvement in BD than this current study however this could be explain by the fact that demographic ,ethnic difference between studies and epidemiological factor were contributing in the development of the disease

In the gynecological aspect 86% of the patients had genital ulcer and this is within agreement of those illustrated by(Ulker. et al, 2007,Erkan et al 2007 and kerkeni. etal, 2010),further more the labia majora was the mostly affected site by current study and this result was confirmed by (Aysel. et al, 1997 ,Suna. et al, 2012 and Virendra. et al, 2014),while only quarter of the patient healed with scar formation again scarring was found with the same percentage in that reported by (Virendra .et al ,2014 and Amal. et al ,2015), the difference between this type of the study and other type of studies was not surprising taken into consideration the lack of the objective criteria ,total sample size, that mostly affected by the different modality of the treatment which actually reflect its affect on the gynecological result

The considerable association between genital ulceration and the mucocutaneous lesion may be due to the pathogenesis of theses lesion, however further studies are recommended to illustrated the gynecological aspect of the BD

In relation to the pathergy test, current study result similar that showed by (Sharquie. et al ,2002).while different results were obtain by other studies (ulker. et al, 2007 ,haruko .etal, 2011,Seyedeh. et al ,2014 and Virendra. et al ,2014)

The pathergy reaction can be vary according to how it done ,the number of pricking ,the characteristics of the needle that is used whether the skin is cleaned , a surgical cleaner before the application and the type of the material injected into the skin

The family history percentage was recorded in this study similar to that showed by Aswad. 2003 while a different percentage were recorded by (Aysel, et al 1997 and Seyedeh. et al, 2014)

This could be explained by the fact that highly predisposing factor could be demonstrating by HLAB51 which may influence it the affect of other members of the family, however the transmission of this disease from one pedigree to another may show mutation furthermore the environmental factor also contributed to the phenotype changes of BD. However extensive studies recommended to demonstrate HLAB51 of the family of the affected person

6. Conclusion

This study showed that a higher rate of female with behcets disease have gynecological involvement with scaring evidence , therefore gynecological examination is mandatory of female with behcets disease

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