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The role of CCL22 and CCL5 in gastric tumor cell metastasis

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ABSTRACT

Background: Gastric cancer is single of the greatest complex types of tumor in Iraq, because it is usually diagnosed late later the tumor takes extent to additional portions of the body. To the identification of some immunological indicators and their part in the development of cancer, the existing training stood conducted to evaluate CCL22 and CCL5 immune histologically and determine their role in metastasis of GC.

Methods**:** Serum concentrations of CCL22 and CCL5 were determined in cases of GC after and before tumor eradication using ELISA kits, and the examination was carried out rendering to the constructer's commands, while those indicators stood determined in paraffin-embedded blocks of stomach tissues immune histologically using the Immunohistochemistry (IHC) method.

Results: present study included 40 cases of GC with age mean of 55.3 years and most of patients are males (60%). We found most of the patients in the fourth (70%) and third stages (25%), in which the cancer is considered to be in the advanced stage. IHC assay determine that CCL22 and CCL5 are highly expressed in gastric cancer cells. Serologically, CCL22 and CCL5 were significantly higher ($p<0.05$) among cases before surgery (19.38 and 21.41 pg/ml) than after surgery (5.01and 6.79 pg/ml) and healthy controls (0.628, 5.053, 6.181 and 7.22 pg/ml) ($p<0.05$). This study found the highest concentration of CCL5 after and before surgery in advanced metastatic cancer cases (stage IV) while the highest level of CCL22 appeared in patients in stage III.

Conclusion: we determined that CCL22 and CCL5 are associated histologically and immunologically with GC, which could be indicators for GC metastases and a target for its treatment.

Key words: CCL22, CCL5, gastric cancer, metastasis, immunohistochemistry

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INTRODUCTION

Stomach cancer, also known as Gastric Cancer (GC), continues to be a significant contributor to cancer-related mortality globally [1]. The incidence of GC varies widely across different geographical regions, suggesting a potential influence of environmental and genetic factors. The primary risk factors associated with distal gastric tumour comprise infection with Helicobacter pylori (H. pylori) and nutritional features, while gastro-oesophageal reflux illness and fatness are also implicated in the progress of proximal intestinal tumour [2, 3]. Over the past few years, extensive research has identified and evaluated various molecules for their clinical significance in the management of GC. Immune response represented by antibodies, immune cells and chemokines has extremely high monitoring value for cancer prognosis [4].

Chemokines stay a set of minor proteins that are secreted and can be categorized into four subfamilies founded on the preserved N-terminal cysteine remains in their sequence: CCL, CD, C, and CX3C. Multiple studies have provided evidence that chemokines and their corresponding receptors production a causative part in cancer metastasis [5]. Among these chemokines, CCL5 and CCL22 have been identified as immunological markers and are downstream objectives of the NF-κB pathway. These chemokines are known to stimulate cancer cell propagation, invasion, and angiogenesis by facilitating the recruitment of eosinophils, monocytes, T cells, and basophils [6, 7].

Angiogenesis, the construction of novel blood vessels, productions a critical part in cancer growth and invasion. CCL5, also known as RANTES, uses proangiogenic properties through stimulating endothelial cell

immigration, dispersion, and neovessel construction, while also improving the appearance of Vascular Endothelial Growth Factor (VEGF). Cancer cells and tumour-related Fibroblasts (CAFs) are the primary sources of CCL5 secretion in the cancer micro-environment (TME). CCL5 attracts various immune cells, including eosinophils cells, monocytes, and mast cells, to the TME [8].

CCL5 contributes to cancer progression through multiple mechanisms. It prompts cancer cell propagation by activating the mammalian objective of rapamycin (mTOR) pathway and enhances ATP manufacture. CCL5 also promotes cancer cell immigration and offensive by activating αvβ3 integrin and upregulating matrix metalloproteinases-2/9 (MMP-2/9). Moreover, CCL5 plays a role in angiogenesis by inducing the secretion of VEGF. Directing the CCR5/CCL5 axis can reprogram the immune-suppressive M2-type cancer-related macrophages (TAMs) into an anti-tumoral M1-TAM phenotype, which enhances the anti-cancer immune response [8, 9].

Previous investigations have indicated that CCL22, primarily interacting with its receptor CCR4, is often associated with adverse factors such as Tregs migration, cancer progression, metastasis in various cancer kinds comprising lung tumour, ovarian tumor, and breast tumor [10]. However, the specific significance and underlying mechanisms of CCL22 appearance in gastric tumor remain poorly elucidated [11]. Cytotoxic T cells (CTLs), known for their anti-tumor immune response, are also current in the cancer micro-environment. The appearance of CCL22 has been proposed to contribute to CTL suppression in cancer by promoting the expression of Tregs [12]. Remarkably, previous research demonstrated complete rejection of melanoma with approximately 99% depletion of Tregs. Another study observed that great permeation of Foxp3+ Tregs and little permeation of CD8+ T cells correlated with CCL22 expression, suggesting its potential immunosuppressive effect. Hence, it is plausible that a like apparatus comprising CCL22 and CCR4 could contribute to immune avoidance in gastric tumor [13]. In this context, our study aims to examine the character of CCL22 and CCL5 in the incidence and metastasis of gastric tumour among Iraqi patients

MATERIALS AND METHODS

Study strategy and data collection

The present investigation is designed as a case-control training involving a entire of 40 patients (16 females and 24 males) selected from multiple hospitals in Iraq between March 2022 and January 2023. Another group of 40 individuals (21 males and 19 females) without any record of systemic illness, clinically identified as healthy, were included by means of the control grouping. The training followed to the ethical guidelines of Al-Diwaniya city, and verbal educated agreement was attained from entirely contributors. The samples collected for investigation consisted of 3 ml of serum collected in plain tubes, as well as paraffin-embedded stomach tissue.

Classification of Gastric Cancer

In present study, Gastric Cancer staged study The specialist furnishes information regarding the size of the tumor using a scale of 1 to 4, assesses the involvement of lymph nodes as N0 to N3, and determines whether the cancer has spread or metastasized as M0 or M1. Smaller numbers indicate a less advanced stage of cancer.

Immunological study

The reagents preparation and assay procedure were carried out according to manufacturer's description of ELISA kits (Solarbio /China)

Immunohistochemistry assay

Previously paraffin-embedded block tissue samples were used to determine specific antigen of CCL5 and CCL22. IHC protocols were performed according to manufacturer's procedure using specific IHC kits (Solarbio/China).

Statistical investigation

The data underwent statistical investigation by means of the SPSS (Statistical Packages for Social Sciences) software, specifically version 19, in addition to the Excel 2010

program, and the probability value smaller than 0.05 was considered to be significantly different.

RESULTS

The current case-control training involved a entire of 40 patients diagnosed with gastric cancer, comprising 24 males and 16 females, as presented in Table 1. The age of the sick extended from 31 years to 78 years, with an average age of 55.3 years (standard deviation ± 13.39). In comparison, the control group consisted of 40 apparently healthy individuals, comprising 21 males and 19 females, with ages extending from 30 to 75 years and an average age of 56.5 years (standard deviation ± 11.66), as illustrated in Table 2. Greatest of the malignant cases stood in the age grouping 64 years to 78 years with a rate of 37.5%, followed by the age group from 42 to 53 with a rate of 22.5%. We also found that males are more susceptible to gastric cancer than females by 60% and 40%, respectively.

Tab. 1. Distribution of patients with intestinal tumor over age and gender

Age Groups (years)	number of Males	number of Females	Total number (%)
31-42	5	3	8 (20%)
42-53	5	4	9 (22.5%)
53 - 64	6	2	8 (20%)
64-78	8	7	15 (37.5%)
Total	24 (60%)	16 (40%)	40

Tab. 2. The case-control comparison according to the age mean.

Case-control comparison			
Age (years)	**Healthy controls**	**Cases**	**p-value**
Range	(30-75)	(31-78)	
Mean	56.5	55.3	0.852 [NS]
SD	11.66	13.39	
SE	1.844	2.117	
Gender			
Males (%)	24 (60%)	21 (53%)	0.161 [NS]
Females (%)	16 (40%)	19 (47%)	0.163 [NS]
N.	40	40	

Our study showed that most cases of GC in our society are diagnosed and treated after it reaches advanced stages, as we found most of the patients in the fourth (70%) and third stages (25%), in which the cancer is considered to be in the advanced stage, while we found only 5% patients in the second stage moreover we did not record any cases in the first stage as in Figure 1.

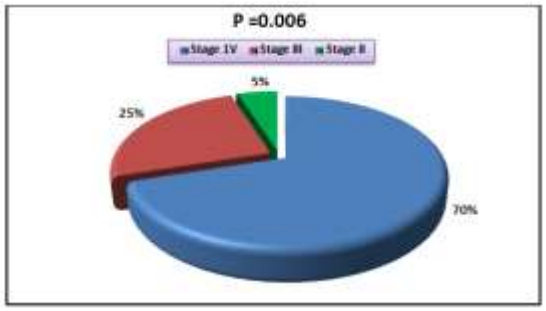

Fig. 1. Frequency of gastric cancer stages

Immunohistochemistry evaluation of CCL22 showed highly expressed in gastric cancer. CCL22 protein was expressed positively in all cases of gastric carcinoma and poorly differentiated malignant cells which deeply staining with chromogen as in Figure. 2. Serologically, the average serum concentration of CCL22 significantly higher ($p<0.05$) among cases before surgery (19.38 pg/ml) than after surgery (5.01 pg/ml) and healthy controls (5.053 pg/ml) as shown in Table 3. Although the concentrations remained high after the surgery, we did not find a statistical difference when comparing the serum concentration of postoperative CCL22 ($p=0.911$) compared to the control.

We found not clear differences ($p>0.05$) when distributing CCL22 concentrations according to age groups, indicating that age affects CCL22 concentrations. Prior to surgery, the age group with the highest concentration of CCL22 (20.02 pg/ml) was found. Patients aged 64 years to 78 years old had the highest concentrations of CCL22 (5.55 pg/ml) after surgery. However, when we divided the concentration of CCL22 according to age after surgery Table 4 there were no discernible differences ($p>0.05$).

The level of CCL22 concentration increased before surgery in the third stage (23.47 pg/ml), while after surgery it was high in people who had cancer in the fourth stage (5.37 pg/ml). In addition, we found clear differences ($p=0.048$) in the distribution of immune marker concentrations by stage. However, statistical differences ($p<0.05$) appeared when comparing the concentration

of each of them before and after surgery for each stage, as shown in Table 5.

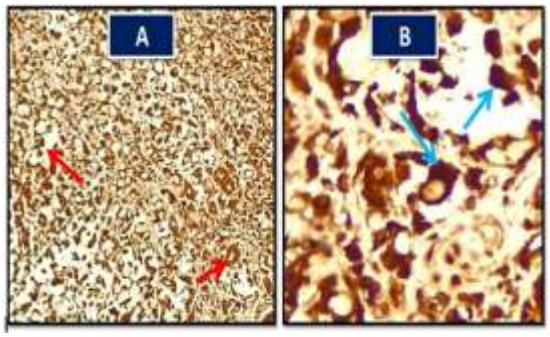

Fig. 2. IHC results of CCL22. A; shows poorly differentiated malignant cells; red arrow (malignant cell) (10X). B; shows poorly differentiated malignant cells; blue arrow (malignant cell) (40 X). Poorly differentiated malignant cells which deeply staining with chromogen

Tab. 3. Comparison serum concentration of CCL22 of studied groups

Serum conc. pg/ml	Case-control comparison		p-Value
	Before surgery	After surgery	
CCL22			
Range	14.21 – 23.44	3.72 – 5.458	0.006 [S]
Mean	19.38	5.01	
SD	2.465	0.078	
SE	0.39	0.12	
	Before surgery	**Control**	
Range	14.21 – 23.44	4.881 – 5.113	0.011 [S]
Mean	19.38	5.053	
SD	2.465	0.159	
SE	0.39	0.025	
	After surgery	**Control**	
Range	3.72 – 5.458	4.881 – 5.113	0.911 [NS]
Mean	5.01	5.053	
SD	0.078	0.159	
SE	0.12	0.025	

Tab. 4. Mean of serum concentration of CCL22 according to patients age groups

Immunological markers (pg/ml)		Age (years) Groups Mean of concentration (pg/ml)				X^2	p-value
		31-42	42-53	53 - 64	64-78		
CCL22	Before surgery	18.81	19.24	20.02	19.71	4.212	0.331 [NS]
	After surgery	4.11	5.33	4.09	5.55	0.81	0.053 [NS]
	P value	0.011 [S]	0.020 [S]	0.002 [S]	0.005 [S]		

Tab. 5. Mean of serum concentration of CCL22 according to cancer stages

Serum conc. pg/ml		Gastric cancer stages Mean of concentration (pg/ml)			p-value
		Stage 2	Stage 3	Stage 4	
CCL22	Before surgery	14.5	23.47	18.75	0.048 [S]
	After surgery	4.89	4.44	5.37	0.355 [NS]
	p-value	0.021 [S]	0.0101[S]	0.023 [S]	

The mean serum concentration of CCL5 were significantly higher ($p<0.05$) among cases before surgery (21.41 pg/ml) than after surgery (6.79 pg/ml) and healthy controls (6.181 pg/ml) as shown in tables (6). Although the concentrations remained high after the surgery, we did not find a statistical difference when comparing the serum concentration of postoperative CCL5 ($p=0.077$) paralleled to the control.

The highest concentrations of CCL5 (28.6 pg/ml) were in the elderly within the age group of 64-78 years. Where we found clear differences ($p=0.033$) when distributing CCL5 concentrations according to age groups as shown in table (7). Moreover, the highest concentrations of CCL5 (6.52 pg/ml) after surgery determine in patients with age range 31 year-42 year. However, we did not find clear differences ($p>0.05$) when distributing the concentration of immunological indicator according to age after surgery.

We found a high concentration of CCL5 after and before surgery in advanced metastatic cancer cases (stage IV), where the level before surgery were 28.6 pg/ml and after surgery 7.55 pg/ml. However, statistical differences ($p<0.05$) appeared when comparing the concentration CCL5 before and after surgery for each stage, as shown in Table 8.

In order to examine the prospective association among elevated serum CCL5 levels and histological abnormalities in gastric tumor, we conducted immunohistochemically (IHC) stain of CCL5 on clinical testers (refer to Figure 3). The findings from this investigation revealed a important upregulation of CCL5 expression in the prime gastric tumor locations, which consequently leads to increased levels of circulating CCL5.

Tab. 6. Comparison serum concentration of CCL5 of studied groups

Serum conc. pg/ml	Case-control comparison		p-Value
	Before surgery	After surgery	
CCL5			
Range	16.23 - 28.67	5.48 – 7.48	0.0058 [S]
Mean	21.41	6.79	
SD	2.466	0.1	
SE	0.379	0.016	
CCL5	Before surgery	Control	
Range	16.23 - 25.67	4.94 - 7.422	0.0047 [S]
Mean	21.41	6.181	
SD	2.466	0.99	
SE	0.379	0.157	
CCL5	After surgery	Control	
Range	5.48 – 7.48	4.94 - 7.422	0.077 [NS]
Mean	6.79	6.181	
SD	0.1	0.99	
SE	0.016	0.157	

Tab 7. Mean of serum concentration of CCL5 according to patients age groups

Immunological markers (pg/ml)		Age (years) Groups				X^2	p-value
		Mean of concentration (pg/ml)					
		31-42	42-53	53 - 64	64-78		
CCL5	Before surgery	18.1	16.9	28	28.6	5.55	0.033 [S]
	After surgery	6.52	5.49	5.77	7.11	1.16	0.292 [NS]
	p-value	0.018 [S]	0.007 [S]	0.003[S]	0.009 [S]		

Tab. 8. Mean of serum concentration of CCL5 according to cancer stages

Serum conc. pg/ml		Gastric cancer stages			p-value
		Mean of concentration (pg/ml)			
		Stage 2	Stage 3	Stage 4	
CCL5	Before surgery	16.27	21.36	28.6	0.048 [S]
	After surgery	5.5	5.32	7.55	0.141 [NS]
	p-value	0.027 [S]	0.011 [S]	0.013 [S]	

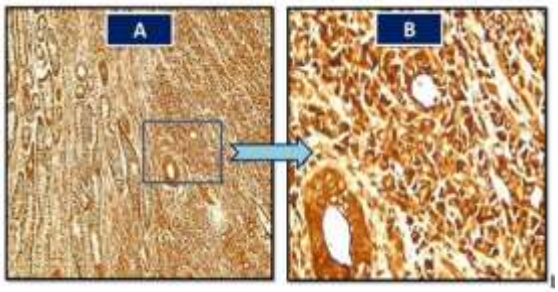

Fig. 3. IHC results of CCL5. Poorly differentiated malignant cells which deeply staining with chromogen (A; 10X and B; 40 X).

DISCUSSION

In this study, age of the sick varied from 31-78 years with an average age of 55.3 years (SD ± 13.39) and greatest of the malignant cases were in the age grouping 64 to 78 years with a rate of 37.5%, followed by the age group from 42-53 with a rate of 22.5%. We also found that males are more susceptible to gastric cancer than females by 60% and 40%, respectively. The average age of the individuals included in the study was

54.44 years. The youngest patient detected with gastric tumor was 24 years old, while the oldest patient was 81 years old [14]. Among the cases examined, there was a higher proportion of males, comprising 45 individuals (58.4%), compared to females, comprising 32 individuals (41.6%). With the aging of the population, there is a tendency for gastric cancer to occur at older ages, a trend that is expected to become more pronounced [15-17] discovered that patients above the age of 40 accounted for 95.1% of all cases, and those over the age of 70 description for 15.2%, which is steady with preceding research findings [15, 16]. The prognosis for patients above the age of 40 is typically poorer than that for younger patients with gastric tumor. Additionally, deprived nutritious status, compromised immunity function, and the presence of long-lasting sicknesses in middle-aged and aging patients might partly explicate the alterations in survival outcomes [17]

A recent study conducted in the United States found that men consistently exhibited a upper occurrence of gastric tumor compared to women, irrespective of competition and ethnicity. This observation has been corroborated by several other epidemiological studies conducted across different regions, including Europe, Asia, and Africa [18, 19]. The disparity in gastric cancer rates between males and females can be attributed to a combination of ecological and hereditary risk features. Helicobacter pylori (H. pylori) infection takes stood identified as the greatest significant danger feature for gastric tumor. The higher prevalence of H. pylori infection in males contributes to an augmented danger of gastric tumor [20]. Smouldering likewise plays a role as a danger feature for gastric cancer, although its impact is relatively weaker compared to H. pylori infection. The relationship among alcohol consumption and gastric tumor danger be contingent on the flat of alcohol consumption. Recent agreement suggests that modest alcohol consumption might not be related with an increased risk of gastric tumor, but full alcohol consumption does elevate the danger [20, 21]. Consequently, higher tobacco and alcohol consumption among males could contribute to a greater danger of gastric tumor. A meta-analysis has sustained the postulate that extended contact to the oestrogen influences, whether of ovarian or exogenous origin, might reduction the danger of gastric tumor [22]. The exact fundamental causes are not yet perfect, but several apparatuses take stood proposed. It has been suggested that oestrogen may enhance the appearance of trefoil feature proteins, which can defend mucous epithelia or prevent the appearance of oncogenes [23].

CCL22 and its receptor CCR4 are implicated in various pathological conditions. Inflammatory diseases mediated by T cells often exhibit high expression of CCL22 in the associated lesions. CCR4, initially identified as differently articulated via Th2 cells complicated in humoral immunity and allergic replies, likewise productions a significant part in cancer progression and metastasis. Consequently, the pharmaceutical industry is actively developing CCR4 receptor antagonists and anti-CCR4 antibodies [24, 25]. Notably, Ménétrier-Caux reported in 2012 that several types of solid cancer cells, comprising ovarian, prostate, breast, gastric, and oesophageal cancer cells, release CCL22. In cancers where CCL22 construction is absent, Tregs do not permeate, irrespective of whether these cancers create further chemokines that bind to CCR4, for instance CCL17. Hence, CCL22 production is essential for the employment of Tregs into the cancer microenvironment [26].

The outcomes of our training displayed that CCL22 stood highly concentrated in the serum and tissues of patients before tumor excision, compared to healthy subjects and/or patients after surgery. We also found that his immune level is relatively close in all age groups, genders and stages after surgery while we found clear differences in level of CCL22 in CG stages before surgery. In the same field, elevated circulating CCL22 levels in research [27]. Peritoneal metastasis and primary reappearance in Gastric Cancer (GC) patients take stood associated with the recruitment of regulatory T cells (Tregs), and CCL22 has been implicated in this process. This suggests that targeting CCL22 may hold potential as a future therapeutic strategy for GC [28]. In the micro-environment of gastric tumor, the presence of CCL17 and CCL22 chemokines is linked to a upper occurrence of Foxp3+ Tregs within Tumor-Infiltrating Lymphocytes (TILs), particularly in the

initial stages of gastric cancer [29]. Demonstrated that the RNA appearance flat of CCL22 in the serum of gastric cancer patients stayed considerably upper paralleled to fit controls ($p<0.05$). Furthermore, the protein expression rank of CCL22 in the serum of gastric cancer patients (1401.67 pg/ml ± 481.12 pg/ml) stayed notably upper than that in healthy controls 500.08 pg/ml ± 100.51 pg/ml ($p<0.05$). Moreover, the increase in CCL22 protein expression level in the serum corresponded to the clinical stage of gastric cancer. Moreover, CCL22 demonstrated a dose-dependent induction of migration in gastric tumor cells [29]. It was recommended that a CCL22 polymorphism is related with an increased danger of rising H. pylori infection-related gastric carcinoma [30].

In accordance with our findings, Wu and colleagues have also observed that CCL22 can serve as a predictive feature for the diagnosis of phases II/III gastric tumor (GC) patients undergoing 5-fluorouracil treatment and chemotherapy [31]. Abnormalities in miR-130a-5p and CCL22 were observed in GC tissues and cells. It was suggested that miR-130a-5p may exert a negative controlling influence on CCL22, and mutually molecules showed diagnostic potential for GC [32]. Exploring early and specific recognition markers for GC has been shown to provide valuable insights into precancerous lesions [33]. Furthermore, recent research has demonstrated that vaccines directing CCL22 can prompt the infiltration of CD8+ T cells and M1 macrophages into the cancer micro-environment, thus augmenting the anti-tumor capabilities in vivo [34].

Consistent with outcomes from a previous study [35], our observations revealed raised rank of serum CCL5 in patients with gastric tumor, mainly those in progressive stages, such as phase IV. Like outcomes stayed described in a regiment of gastric tumor patients in Iran [36]. The group of patients with high levels of CCL5 exhibited further progressive illness and a higher proportion of persons with deprived or undistinguishable tumor. Furthermore, our study established that pre-surgical serum CCL5 rank could serve as a predictive marker for occult peritoneal metastasis.

In relation to the involvement of CCR5/CCL5 in gastric tumor, numerous trainings have established the appearance of CCR5 and its ligand in gastric tumor cells together in vitro and in vivo. CCR5 expression on the cell membrane has been observed in various gastric cell lines, comprising MKN45, MKN74, and KATO III, at both the RNA and protein ranks [36]. Immunostaining of human gastric cancer tissue confirmed the differential expression of CCR5, and its expression was found to be related with lymph node metastasis and a poorer diagnosis in patients with gastric tumor [37]. Moreover, CCR5 expression was identified as an independent indicator of an unfavourable diagnosis in gastric tumor. Additionally, Gawron et al. reported that a CCR5 haplotype comprising communal alleles, such as IVS1+151 G>T (rs2734686) and IVS2+80 C>T (rs1800024), along with the slight allele IVS1+246 A>G (rs1799987), stood temperately related with an augmented danger of gastric tumor. It has been observed that gastric cancer cells produce CCL5/RANTES, and upper serum concentrations of RANTES are related with additional progressive phases of gastric tumor [38].

Recently, it has been reported by Ding et al. that CCL5 concealed via cancer related macrophages might donate to the propagation, offensive, and metastasis of gastric tumor cells. In their training, high expression levels of CCL5 and CD68, which are surface indicators of cancer related macrophages, were observed in gastric tumor tissue, and their expression ranks showed a positive correlation. Moreover, the expression of CCL5 and CD68 stayed considerably related with the depth of attack, lymph node metastasis, performance, and cancer distinction [39]. Co-culturing AGS gastric tumor cells with macrophages derived from THP-1 cells resulted in improved propagation, movement, and clone-forming capacity of the gastric tumor cells. This co-culture also upregulated the expression of CCR5/CCL5 and phosphorylated signal transducer and activator of transcription 3 (p-Stat3), indicating that the stimulation of Stat3 and the stimulation of the CCR5/CCL5 axis may play a critical part in gastric tumorigenesis [39]. Okita et al. have recommended that gastric tumor cells gain offensive properties concluded cooperation with peripheral blood

mononuclear cells, with CCL5 playing a significant part in this process [40].

Recently, in a training directed by Kim et al. in 2003, it stayed discovered that individuals with stage IV gastric cancer exhibit a considerably elevated serum CCL5 level in comparison to those at earlier stages [41]. Moreover, CCL5 triggers the activation of PI3K, Akt, and NF-κB pathways, which, in turn, enhance the migration of lung cancer cells. This indicates that CCL5 may facilitate the dissemination of gastric cancer to distant areas through comparable molecular mechanisms. Leukocytes within the cancer stroma play a crucial role in supporting growth growth and metastasis. CCL5 specifically attracts leukocytes articulating CCR5 to the cancer micro-environment, thereby promoting tumor progress [42].

Based on a study conducted by Aldinucci et al. in 2018, the prolonged inflammation in the stomach, resulting from H. pylori infection and the construction of inflammatory intermediaries, cytokines, and chemokines, including CCL5 in gastric tissues, has a significant influence on the onset and advancement of gastric tumor [43].

Researchers, specifically Sugasawa et al., have conducted studies showcasing that gastric tumor cells stimulate the expression of CCL5 in nearby lymphocytes. This, in turn, not only facilitates the propagation of gastric tumor cells but likewise inhibits the anti-tumor immune reaction via triggering heightened apoptosis of nearby cytotoxic T lymphocytes. Therefore, Sugasawa et al. have provided evidence demonstrating that CCL5 promotes the advancement of tumours while impeding their removal via the host immunity system [35]. Additionally, Sugasawa et al. have identified a new mechanism by which gastric tumor cells acquire increased proliferative action and evade the host's anti-tumor immune response through the induction of elevated CCL5 expression [35]. However, further fundamental examinations are requisite to improvement a precise considerate of the mechanisms underlying the part of CCL5 in gastric tumor

Our study did not show a role or effect of age or the sex of the patient on CCL22 concentration, although its concentration increased slightly in females and persons aged fifty or more. To explain this, we think that female hormones have a role in influencing some chemokines, such as CCL22, in addition to the psychological state and the biological nature of women contribute to the emergence of this result. On the other hand, the failing of the immunity system with age and the stresses of life may be due to the fluctuation or deterioration of some immune indicators including CCL22. However, we did not find studies dealing with this topic in order to obtain an explanation for these cases. Therefore, we may need a broader study that includes a larger number of patients in determining the A level according to gender or age.

CONCLUSION

We found that most of the patients with GC in our population were diagnosed with cancer in late stages, especially in males, and we determined that CCL22 and CCL5 are associated histologically and immunologically with GC, which could be indicators for metastasis the GC and a target for its treatment

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