REVIEW

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Malignancy of Malignant Ascites: A Comprehensive Review of Interplay between Biochemical Variables, Tumor Microenvironment and Growth Factors

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Abstract

Malignant ascites, a buildup of fluid in the abdominal cavity, is a serious consequence of many malignancies. This review aims to comprehend the biochemical makeup of malignant ascites, such as pH, cholesterol, protein, etc., which is crucial to developing therapeutics with better treatment outcomes and hence correlate with corresponding prognostic value. The unique tumour microenvironment exhibited by malignant ascites and the crosstalk between inflammatory cells, cytokines and chemokines, interactions between tumour and non-tumour cell types, activation of vital cell signalling pathways within the TME for VEGF-regulated sustained angiogenesis, cancer progression and metastasis is highlighted. This review addresses the need to develop comprehensive assay platforms to identify various biochemical aspects of ascites, to discover the interactions of the tumour microenvironment and to study VEGF-regulated permeability that can expedite early diagnosis and progression of ascites.

Keywords: Ascites- malignant ascites- ovarian cancer- tumour microenvironment- cholesterol- lysophosphatidic acid

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Introduction

Ascites is a condition characterised by inflammation that causes an excessive buildup of fluid in the abdomen. This state is seen in many neoplasms involving peritoneal spread. In virtually all patients, recurring illness is followed by the formation of malignant ascites, which is a serious clinical problem that numerous individuals having advanced disease face, causing discomfort and distress [1].

The peritoneal dispersion complicates the intricate mechanisms underlying ascites development. Tumor growth leads to increased fluid filtration due to the expansion of the cross-sectional area of microvessels lining the abdominal cavity. Tumors also induce a pro-inflammatory response in the abdominal cavity, facilitating the adhesion of tumor cells to the peritoneal surface and intraperitoneal organs. In addition to various anatomical and physiological factors, retrograde lymph flow can accelerate the formation of ascites [2]. The complex pathophysiology of malignant ascites is closely correlated with its progression. Malignant ascites facilitates trans-mesothelial invasion by cancer cells. Additionally, it accelerates the senescence of normal peritoneal mesothelial cells, leading them to adopt traits that support cancer development (Figure 1).

Ascites is one of the most important determinants in the formation of ovarian malignancies, especially when it comes to distant organs and peritoneal metastases [3].

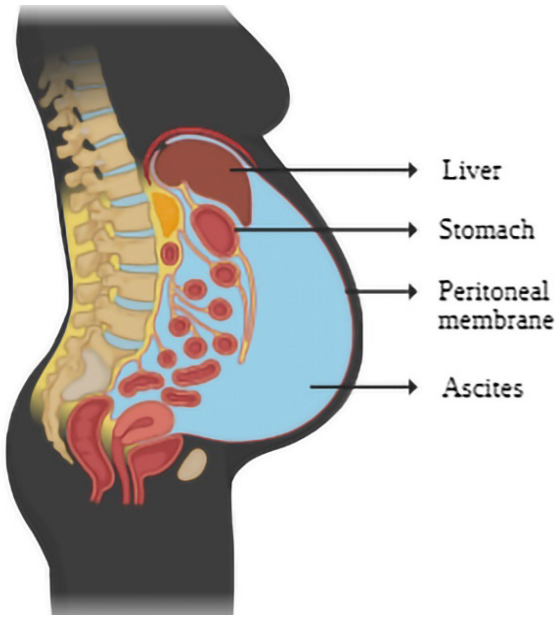

Figure 1. Illustration of Ascites Buildup in the Abdomen of a Female

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Though ascites is most prominent in patients with III and IV stage of ovarian cancer, it occurs at the time of initial diagnosis in nearly one third of patients, offering a chance to constantly collect the tumour cells. Although ascites is believed to play a significant part in the metastatic process, studying its constituents may help us understand the mechanisms behind the spread of cancer cells, which may lead to new avenues for management and improved patient prospects [4]. It can be differentiated by its biochemical composition, such as pH, cholesterol, etc. which are crucial in their identification and classification.

According to Rickard BP et al. [5], the cellular components of malignant ascites include stromal cells, inflammatory cells, endothelial cells, and cancer cells, which are often detected as single cells or spheroids. Furthermore, proteins, various metabolites, and cytokines like interleukin (IL)-6 and IL-8 are examples of acellular factors. Their complex combination creates a milieu for the tumour, affecting tumour cell growth, progression, chemoresistance, and immune evasion, indicating that malignant ascites actively participates in the advancement of several malignancies. The hallmark of ascites, a significant tumor microenvironment (TME), is the accumulation of excess fluid in the abdomen, primarily due to obstructed lymphatic channels and increased microvascular permeability [6, 7]. A change in vascular permeability has been suggested as a possible aetiology for the development of ascites. The levels of VEGF, a powerful angiogenic protein, are noticeably increased in malignant ascites which increases the permeability of cells called endothelial cells [8]. The objective of this study is to offer an in-depth review of the biochemical constituents present in ascitic fluid, identify interactions in the tumour microenvironment, and the growth factors that aid in tumour metastases (Figure 2).

Biochemical variables

Biochemical investigations of peritoneal and pleural fluid samples are often performed in clinical labs. Typically, the objective is to identify the cause of ascites. Biochemical markers such as total ascitic protein, ascitic albumin, LDH, and cytokines (IL-6 and VEGF) are essential diagnostic and therapeutic indicators in people with malignant ascites. These signs can assist differentiate between malignant and non-malignant ascites, in addition to the stage of the illness along with therapy efficiency [9]. Below are few important components of malignant ascites;

pH

According to several types of research, individuals with malignant ascites showed low ascitic fluid pH levels (7.39+/-0.07). It is due to the hypoxic conditions that lead to the production of acidic metabolites like lactic acid which further leads to inflammation, rapid and uncontrolled tumour cell proliferation. This in turn encourages the sustenance and invasion of tumour cells and possibly impair the immune system of the body. Therefore, serves to be an important clinical diagnostic marker [5].

Lactate Dehydrogenase (LDH)

Lactate Dehydrogenase as a critical distinguishing factor between malignant and non-malignant ascites.

LDH plays a critical role in the ascites differential diagnosis, particularly when trying to distinguish between benign and malignant aetiology. According to research by Du et al. [11], elevated levels of lactate dehydrogenase (LDH) in the ascitic fluid are thought to be strongly associated with the malignant form of this condition. As a result, LDH can be regarded as a crucial marker in the ascites diagnostic criteria. Malignant cells have a different metabolism than normal cells, which affects the amount of LDH, an inducer of anaerobic glycolysis. As with ascites LDH, increasing levels imply the cellular turnover and necrosis linked with cancers. These findings are corroborated by research issued in the Journal of the Indian Academy of Clinical Medicine (2021), which claims that LDH, along with CA125 and CEA, is a crucial diagnostic sign. Therefore, ascitic fluid LDH levels can be measured to accurately assess the likelihood of malignancy

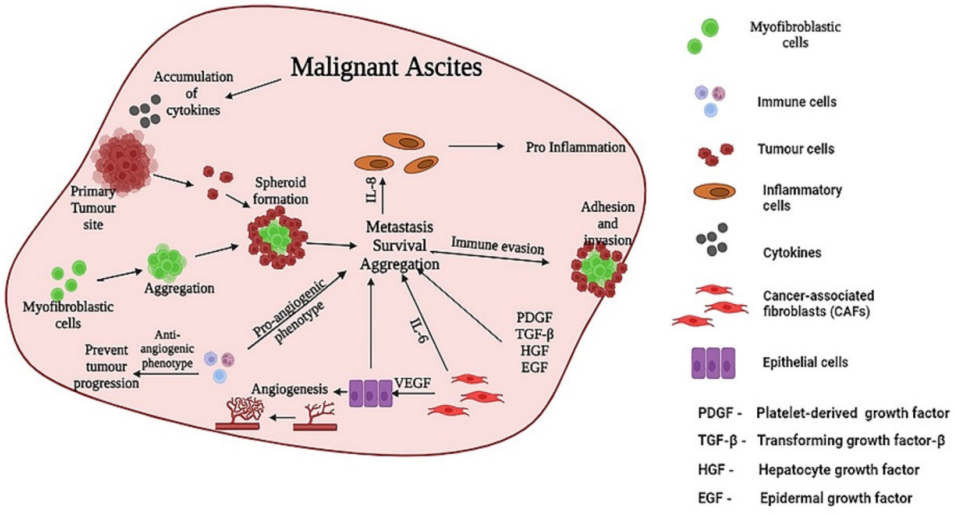

Figure 2. Representation of the Complex Interplay of the Tumor Microenvironment Comprising Tumor Cells that Secrete Pro-Tumoral Cytokines and Chemokines, Growth Factors Leading to Metastases and T tumor associated Immunity

and to promptly identify peritoneal carcinomatosis while formulating an appropriate treatment plan. These studies underline that, in order to improve diagnosis, LDH can be helpful when used in conjunction with other ascitic analysis of fluids procedures [10, 11].

Serum Ascites Albumin Gradient (SAAG)

The level of SAAG can be determined by subtracting levels of ascites albumin from the serum albumin concentration. In presence of portal hypertension, osmotic pressure gradient between plasma and ascitic fluid has to be raised to counterbalance the high hydrostatic pressure driving the fluid into the intra-peritoneal cavity. SAAG, the single most important factor of osmotic pressure generation, is used to differentiate ascites into two categories: High SAAG ascites (SAAG >/= 1.1 g/dl in cases with portal hypertension) and Low SAAG ascites (SAAG < 1.1 g/dl in cases with ascites unrelated to portal hypertension). Numerous investigations have shown that the serum ascites albumin gradient is more effective in categorising ascites than protein content or other variables used in ascitic fluid analysis. Study conducted by Mandala and Krishna clearly demonstrate that SAAG offers an excellent discrimination of the causes of ascites. Similar observations have been reported by other studies too [12].

Proteins

According to Kipps et al., the aetiology of the ascites can be better understood by examining the protein profile of the pathologic condition [13]. A recent study on the biochemical characterization of proteins in ascites showed that the ascites of benign aetiology comprised of 1855 different types of proteins as compared to 2096 distinct kinds of proteins in the ascites of malignant ascites. Compared to benign ascites higher expression levels of mesothelin (MSLN), glyceraldehyde phosphate dehydrogenase (GAPDH), and pyruvate kinase isozymes M1/M2 (PKM1/2) was observed [14]. Another interesting fact is the presence of elevated exosome levels in malignant ascites. Numerous proteins that have been discovered to be specifically associated with malignant ascites constitute intracellular proteins that may be transported from cells within exosomes which interestingly are elevated in malignant ascites. These exosomes play a crucial role in the transportation of proteins that trigger various pro angiogenic signalling pathways within tumour cells and the surrounding tissues [15].

Tumour markers

Various proteins act as tumour biomarkers for characterization and identification of the aetiology of cancer related ascites. Particularly in individuals with gastrointestinal and ovarian neoplasms, tumour markers in ascitic fluid are useful for peritoneal carcinomatosis diagnosis. Certain indicators can help differentiate between benign and malignant ascites, improving the diagnostic potential. In a different research, Yaewon Yang et al. concentrate on the value of ascitic tumour markers, particularly those related to malignant ascites brought on by gastric cancer. Their research highlights the role of CA125, CEA, and CA19-9 in the diagnosis of peritoneal cancer. In order to emphasise the importance of indicators for the timely detection and treatment of malignant ascites and to assist doctors in developing patient-centered treatment strategies, these markers are emphasised in both trials [16, 17].

Lysophosphatidic acid (LPA)

A bioactive phospholipid, Lysophosphatidic acid, is known to influence membrane permeability and promote buildup of ascites [14]. It has been demonstrated that a poorer prognosis correlates with an LPA-induced gene expression profile [13]. Evidence suggests that these are present in substantial quantities in the ascites of patients who have ovarian cancer [14]. Glycoprotein phosphodiesterase autotoxin (ATX) produced extracellularly mediates G-protein-dependent receptor signalling on the cell surface through LPA that leads to the production of unsaturated fatty acyl chains. These G protein-dependent receptors are activated when ovarian surface epithelial cells undergo malignant transformation. Ascites is produced as a result of suppression of gap junctional communication, and increased endothelial permeability, which is regulated by LPA leading to increased mRNA levels and transcriptional control of VEGFA, urokinase plasminogen activator (UPA), IL-6, and IL-8 [13].

Cholesterol

Identification of cholesterol concentration is a superior tool for the diagnosis of malignant ascites as compared to cytological studies. The composition of malignant ascites was dominated by higher concentrations of cholesterol in comparison with LD and SAAG. Patients with peritoneal malignancies have elevated cholesterol levels and measuring cholesterol helps distinguish malignant ascites from other causes of ascitic effusions. Patients with ovarian cancer exhibit reduced survival rates when confronted with malignant ascites and acquired chemoresistance [18]. Thus, it is evident that the composition of ascites has a great role in the diagnosis of malignant ascites and also in tumour progression.

Tumour Microenvironment (TME)

TME plays a significant role in cancer development, metastasis and contribute to the stabilization of many cancer hallmarks. Tumour cells and TME cooperate to develop sustained angiogenesis, immune cell filtration and stabilization of cell derived vesicles during the early stages of development [19]. Malignant ascites facilitates the dissemination of cancerous cells across pelvic and peritoneal regions. This trans-coelomic dissemination is crucial in adhesion of tumour cells to the omentum and serous membranes that line the peritoneal organs, leading to metastatic lesions in the peritoneal cavity instead of invading the lamina propria like the majority of other solid tumours. Indeed, malignant ascites is necessary for transcoelomic metastasis, contributing to the spread of tumour cells and serving as an environment optimal for growth [1]. Ascites alters the surrounding environment of the abdominal region, having a significant impact on the ways in which particular cell types, organs, tissues, etc. operate [20].

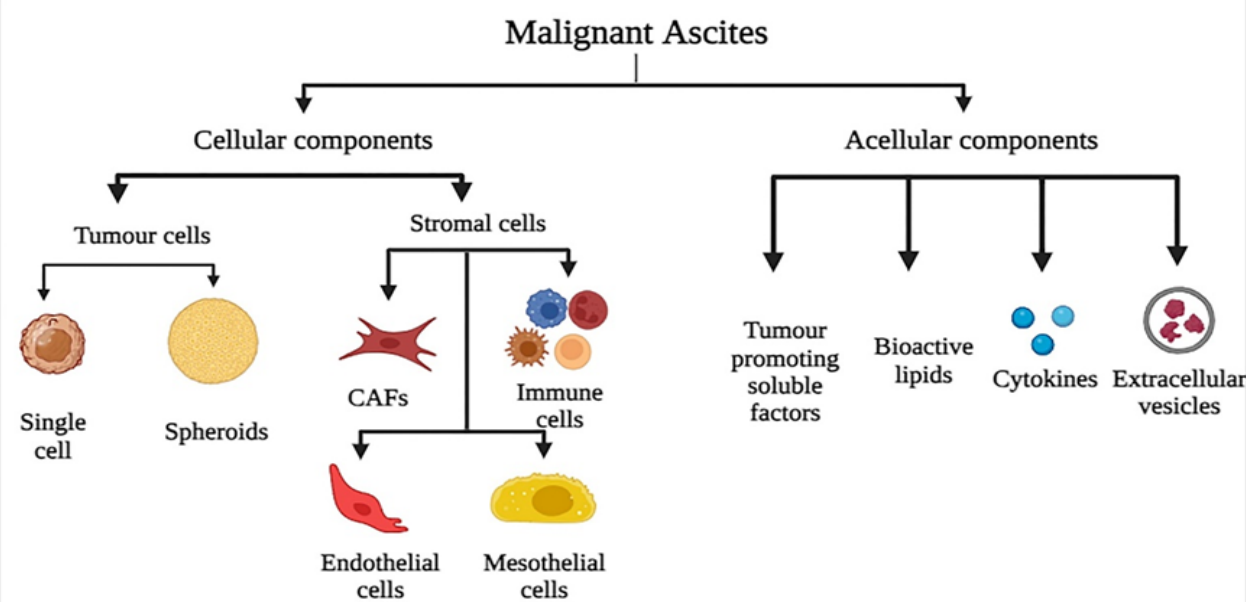

Figure 3. Schematic Representation of Cellular and Acellular Components of Ascites. The tumour and stromal cells of malignant ascites make up its cellular components. The acellular components are made up of cytokines, tumour promoting soluble factors, bioactive lipids and extracellular vesicles

The cell-cell interactions between the TME and neighbouring tissues along with altered gene expression profiles, is primarily due to the unique habitat of malignant ascites that include biological components and active cells [21]. As a result, a huge number of inflammatory cells, cytokines, and chemokines are produced, creating an intricate web that is known to directly influence host cells and further change the environment. Cancer cells and stromal cells communicate with one another via direct cell-cell contact and an indirect cytokine-mediated connection [7]. Migration of cancer cells to the abdominal cavity is furthered by the infiltration of a large number of tumour-associated macrophages (TAMs) in the TME which aid in promotion of angiogenesis, matrix remodelling, and lymph angiogenesis. Therefore, they act as crucial communicators between the inflammatory environment of the tumour and the specific tumour cells. This is primarily responsible for the weakening of immunity and accelerate tumour progression [20]. Deprivation of nutrients like glucose, accumulation of metabolic products like lipids, adenosine, etc, and hypoxia in the TME could inhibit a variety of functions associated with T-cell activation [22]. Interestingly, the immune cell population can contribute to immunosurveillance hindering tumour progression, but also, their crosstalk with TME mediated by several cytokines, growth factors and signalling molecules can modify immune cells to adopt the pro-tumourigenic phenotype. [19].

Two of the primary constituents of ascites, the cellular and the acellular fractions, is suggestive of malignant ascites in the abdomen and their interplay frequently results in sustained angiogenesis contributing to further build up of the fluid. It is also crucial to thoroughly characterize the ascites microenvironment as a distinct compartment, as it is believed to promote reversible dormancy in cancer cells, leading to recurrent disease. Understanding this environment could offer opportunities for improved therapeutic approaches [1, 6].

Cellular components

A complex, diverse collection of cell types, comprising stromal cells and cancer cells, each with a specific function, make up the constituent cells of malignant ascites. The stromal cellular elements include fibroblasts, immune cells, adipocytes, stromal cells derived from adipose tissue, and bone marrow-derived stem cells. Angiogenesis and proliferation are among the abnormal traits exhibited by certain groups of these stromal cellular elements [15]. Cancer-associated fibroblasts (CAFs) in the tumour stromal environment, release regulation factors to both healthy cells and cancer cells, which induce a feedback loop for growth, migration, and chemo resistance [15, 23].

Human peritoneal mesothelial cells (HPMC) release substances (for example- lysophosphatidic acid) that encourage tumour growth, similar to CAFs. It has also been shown that these cancer-associated mesothelial cells release regulation factors that aid ovarian cancer cells in developing chemoresistance. Ascites contains tumour cells that are either present as adherent individual cells or, more often as spheroids which are predominantly responsible for the aggressiveness and high metastatic ability of tumours [15,18]. Screening, concentrating, eliminating cellular components, and reinfusing ascitic fluid are all part of cell-free and concentrated ascites reinfusion treatment (CART), which successfully reduces ascites-related symptoms and enhances patients' overall health [6].

Acellular components

The acellular elements of ascites are impacted by the diverse blending of their cellular components [15]. Patients with ovarian cancer have significantly more natural killer cells (NK) and T lymphocytes in the ascites than in the blood. Thus, it is important to understand

the intricate cell-cell and cell-protein communications between immune cells and tumour cells regulated by cytokines, chemokines, and protein. Proinflammatory cytokine concentrations in ascites are 40–500 times higher than in serum [14]. The tumour microenvironment of ovarian cancer ascites contains pro- -tumourigenic cytokines which include IL-2, IL-5, IL-7, and IL-17, as well as IL-6, IL-8, IL-10, IL-15, IP-10, MCP-1, MIP-1, and vascular endothelial growth factor (VEGF) and also, anti- tumourigenic cytokines. These elements work together to produce an immunosuppressive and pro-inflammatory tumour microenvironment [15, 5] Extracellular vesicles, or EVs, are one aspect of ascites that might facilitate dissemination. They act as mediators of cellular interaction, communicate information in the form of miRNAs, proteins, and lipids, and drive the spread of ovarian cancer spheroids towards omental fat. Notably, FRα, Claudin-3, and TACSTD2 (also called TROP-2) have recently been shown to be HGSC-specific small EV markers. These markers are valuable in isolation of EVs from ascites for early diagnosis of HGSC [24].

In animal models, the expression of IL-8 has been linked to enhanced tumourigenicity and ascites development and IL-6 facilitates angiogenesis, chemoresistance, tumour growth, migration, and invasion [15]. Exosomes are nano-sized microvesicles (30–100 nanometres in diameter) that can travel throughout the body, carry donor cell molecular signatures, transmit information across cells and thus change the gene expression of recipient cells. It is interesting to note that in ovarian cancer patients, the capacity of peripheral blood mononuclear cells to cause cytotoxicity is impaired by exosomes dissociated from the ascites [18]. Higher expression of numerous substances, including angiogenin, angiopoietin-osteoprotegerin (OPG), and urokinase plasminogen activator receptor (uPAR), was observed in the ascites from a few epithelial malignancies. OPG has been identified as a mesothelial and endothelial cell-secreted substance that inhibits TRAIL-induced apoptosis of ovarian cancer cells and promotes tumour development and angiogenesis [15,18]. In ovarian cancer, the portion of ascetic fluid that is acellular creates a protective milieu that aids in the growth of tumour cells and the recurrence of the disease, which encourages de novo resistance of tumour cells [14](Figure 3).

Difference in TME of malignant ascites and solid tumours

Malignant ascites has a unique and considerably different tumour microenvironment than solid tumours. The TME of solid tumours is more organised and structured, whereas TME of malignant ascites is a heterogeneous collection of various components. Targeting tumour cells becomes far more difficult in cases of malignant ascites than it is in cases of solid tumours. A comparison of the kinetic characteristics of solid and ascites tumours originating from the same kind of cell may therefore provide some insight into the variables that affect tumour cell proliferation because solid and ascites tumours have different nutritional conditions. Compared to many solid tumours, where there is evidence that cells may quickly die away after becoming anoxic, cells in ascites tumours appear to be more resistant to anoxia. Peristaltic action of the intestine causes movement of ascites cells within the peritoneum, allowing repeated oxygenation from surrounding vascularized membranes for short periods of their cycle; this may be sufficient to prevent cell death [25]. According to studies, ascites fluid produced as a result of gynaecologic cancers revealed greater levels of expression of lysosomal enzymes such as β-glucuronidase, β-galactosidase, and α-mannosidase, which aids in lysosomal signalling and so helps cancer cells to achieve increased energy requirement. Ascites fluid exhibits a greater concentration of components

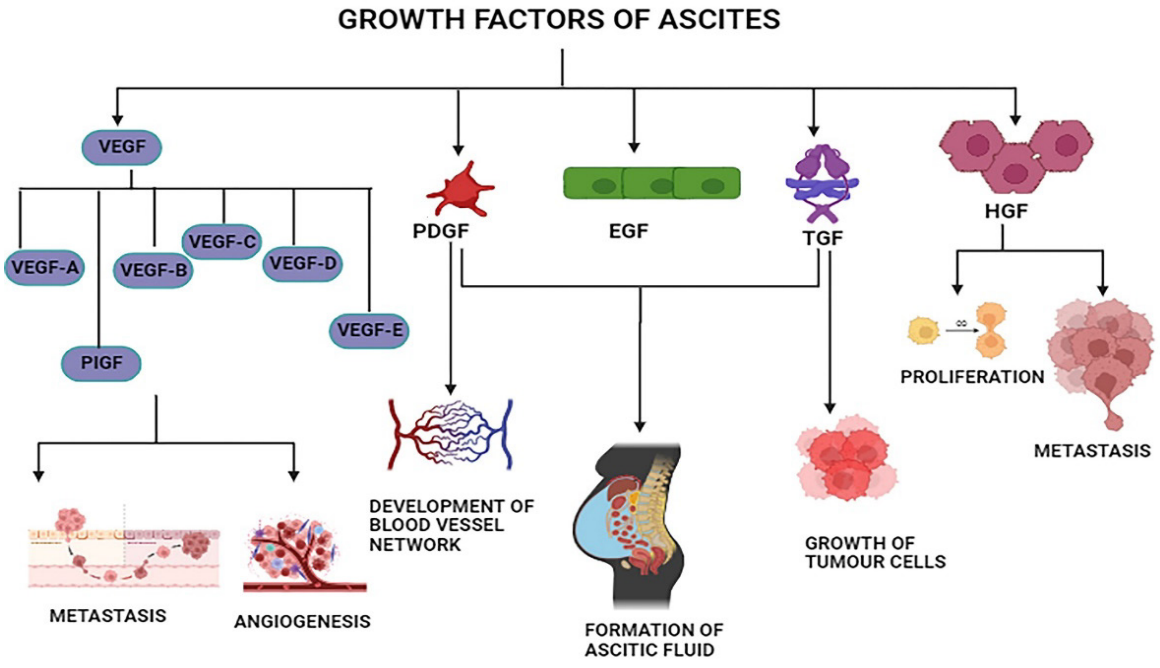

Figure 4. Schematic Representation of Growth Factors of Ascites. (i)VEGF- Vascular Endothelial Growth Factor, (ii) PDGF- Platelet-Derived Growth Factor, (iii) EGF- Epidermal Growth Factor, (iv) βTGF- Transforming Growth Factor-β, (v) HGF- Hepatocyte Growth Factor

associated with cell invasion like MMPs, fibronectin and vitronectin when compared to solid tumours [18].

Integrins and urokinase plasminogen activator receptor (uPAR) expressions are altered by the presence of ascites. This leads to activation of signalling pathways like MAPK and RAS. Evidence for this is the inhibition of MAPK pathway using antibodies against α6 and β1 integrins. Similarly, RAS pathway can be inhibited by using antibodies against urokinase plasminogen activator receptor (uPAR). These findings imply that an increase in α6β1 integrin and uPAR expression caused by ascites affects cancer cell activities by activating oncogenic and survival pathways. This is one of the reasons why ascites tumour is considered more aggressive than solid tumours [5]. Antitumour immunity is reduced in the environment of ovarian cancer ascites, allowing the tumour cells to evade immune surveillance. The immunosuppressive state of malignant ascites is a result of metabolic variables such as hypoxia, limited nutrition, and the buildup of metabolic products. Malignant ascites is hypoxic but not noticeably acidic, in contrast to the hypoxic and acidic environment of solid tumours [18].

Metastatic lesions of solid tumour are found in various organs or tissues depending stage of cancer while on other hand malignant ascites involves the widespread of cancer cells within the abdominal cavity making it difficult to determining the exact origin A challenge when compared to solid tumours, ascites and their contents are not routinely stored for further analysis in biobanks, and volumes are frequently erratically recorded, currently limiting the possibility of large-scale analysis of ascites samples. Treating ascites presents additional difficulties since sample transmission to researchers may take longer than expected because the samples are recovered after a patient has had therapeutic paracentesis. Therefore, it is imperative to take into account how time affects the samples' integrity so legitimate research may be conducted with a defined procedure for managing this special biospecimen. [4].

Growth Factors

The evolution and expansion of malignant ascites are influenced by several variables, including specific growth factors. Platelet-derived growth factor (PDGF) promotes angiogenesis and the proliferation of connective tissue cells that further enhances the accumulation of ascitic fluid [26]. Transforming growth factor-β (TGF-β) alters the TME, promoting tumour survival and Hepatocyte growth factor (HGF) mediates cell invasion, migration, and proliferation of tumour cells [27, 28]. Similarly, epidermal growth factor (EGF) is also a significant contributor of tumour cell survival and development in ascitic tumours because of which many malignancies exhibit over expression of EGF and EGFRs [23].

Vascular Endothelial Growth Factor (VEGF)

VEGF-A, -B, -C, -D, and placental growth factor (PlGF) make up the family of five structurally related molecules in the VEGF family. VEGF signalling is mediated by three receptor tyrosine kinases: VEGFR-1 (Flt-1), VEGFR-2 (KDR/Flk-1), and VEGFR-3 (Flt-4) [3, 29]. VEGF-A, a component of the immunosuppressive network, stimulates angiogenesis and draws immature myeloid cells to the cancer tissue, promoting the growth of tumours. Tumour vessel dilatation, increased permeability, and leakage are the primary characteristics of this sprouting phase, which are caused by the actions of VEGF [8].

Anti-angiogenic treatment is a possible means of preventing ascites. By weakening the tight connections between peritoneal endothelial cells and increasing endothelium permeability, VEGF has been repeatedly linked to the development of ascites. They alter the cell-cell interactions in the ascites and regulate nutrient and energy production for tumour cell survival [23]. Malignant ascites frequently buildup as a result of peritoneal metastasis. The peritoneal cavity has a sophisticated microenvironmental matrix that promotes tumor growth. VEGF is often released by tumor and stromal cells, including macrophages in ascites, along with tumour-infiltrating T cells, aids in metastasis and neovascularization [30, 28].

Employing anti-VEGF antibodies for inhibiting VEGF activity has led to a considerable reduction in the buildup of fluid in the abdominal cavity. Both the development of additional blood capillaries and the permeability of already-existing blood vessels are aided by VEGF. These may result in the creation of ascites, peritoneal carcinomatosis, tumor growth, and tumor dissemination throughout the abdomen. Ascites cause VEGF to build up, which can then cause a reduction in adherens junctions (VE-cadherin) and tight junctions (claudin 5) [31, 23]. Increased serum VEGF levels are associated with advanced tumour stages and can be used as a prognostic biomarker to differentiate malignant ascites from benign ones. Malignant ascites had considerably greater levels of VEGF (676.59 303.86 pg/ml) than benign ascites (218.37 98.15 pg/ml) (P 0.001). Furthermore, it is known that ovarian cancer patients with malignant ascites exhibited greater VEGF levels as compared to other malignancies. Treating ascites through the aid of VEGF involves the use of a fusion protein called VEGF-trap and the mode of action is blocking the interaction of VEGF receptors. In contrast to bevacizumab, which binds to VEGF via an antibody-based method, VEGF-trap, also known as aflibercept, binds to the VEGFR-1 and VEGFR-2 receptors using their third and second binding domains. These extracellular sequences of proteins are fused to the Fragment crystallizable region of a human IgG backbone to generate this chimeric protein. It binds all isomers of the VEGF-A family and has a very high VEGF binding affinity thus contributing to inhibiting angiogenesis, and blocking VEGF signalling, which ultimately reduces the leakiness of blood vessels in the peritoneal cavity which results in considerable resolution of ascites [32] (Figure 4).

In conclusion, this review paper has provided an in-depth analysis of the biochemical components, tumour microenvironment, the role of VEGF in the pathogenesis of malignant ascites and thus highlighted the possibilities of novel targeted therapies. Malignant ascites diagnosis and therapy are strongly influenced by

biochemical factors. LDH, SAAG and LPA levels serve to be important clinical diagnostic parameters. Cholesterol serves as a potential differentiator between malignant and non-malignant ascites, as elevated cholesterol levels is indicative of malignant ascites. Protein levels and tumour markers can also be used to assess the aetiology of malignant ascites.

Drugs targeting Hif signalling (Hypoxia Inducible Factor) could serve as potential candidates to regulate exosome production and transport, thereby inhibiting angiogenic signalling pathways. The TME creates an environment that is conducive to tumour development and angiogenesis through the dynamic interactions between its cellular and acellular components. Novel molecules that target TME by modulating various cell to cell interactions, cytokines, chemokines, which in turn influence antitumour immunity, metastasis and chemoresistance need to be developed. Enumeration of HPMCs in the TME that release pro tumorigenic peptides in response to peritoneal inflammation is a valuable tool to monitor tumour progression. Identification of novel and safe drugs targeting IL-8 and IL-6 could be a potential strategy to combat angiogenesis, ascites development and chemoresistance.

Malignant ascites research is still in its early stages, offering opportunities to learn more about this illness and provide better methods of diagnosis and therapy. Considering the challenges associated with management, diagnosis, and treatment of malignant ascites, novel strategies and technologies need to be developed for better therapeutic outcomes. Drugs that inhibit fluid retention and identification of novel biomarkers in the diagnosis of ascitic tumour is an area that requires immediate attention. With the successful development of sensitive and cost-effective biochemical assay platforms that monitor LDH, SAAG, LPA and cholesterol, aided with existing screening modalities, early diagnosis of ascites driven cancers could be possible. Variations in these biochemical variables facilitate therapy customization and raise the possibility of a customised medical strategy. The TME of ascites tumors are distinctly variable than that of solid tumors. With increasing awareness on TME and its cross talk between the surrounding tissues, deciphering the signal transduction pathways that regulate these cellular communications would be a valuable strategy to control ascites tumour development, antitumour immunity and chemoresistance. Consequently, we derive a conclusion that further extensive study into these targeted therapeutics will be needed for appropriate management of malignant ascites, thereby enhancing the quality of life for patients.

Author Contribution Statement

Remi Jacob: Writing- Original draft preparation; Sangeerthana A: Writing- Original draft preparation; Nadha Abdul Razack: Writing- Revision and editing; Samudyata C. Prabhuswamimath: Conceptualization, Writing- Review and editing, supervision, correspondence.

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Conflict of interest

All authors have no conflicts of interest to disclose.

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