Open Access

OBM Integrative and Complementary Medicine

LIDSEN Publishing Inc.

Original Research

Experiences of Patients With Hashimoto Thyroiditis Through the Lens of Compassion

Zoi Portokalidou [1], Anna Huysse-Gaytandjieva [2,*], Madelon L. Peters [3]

1. Independent Researcher, Leiden, The Netherlands; E-Mail: zoiportokalidou@gmail.com
2. Psychotherapie Praktijk Limburg; Hashimoto.Help, Brightlands Health Campus, Gaetano Martinolaan 85, 6229 GS, Maastricht, The Netherlands; E-Mail: info@hashimoto.help
3. Department of Clinical Psychological Science, Faculty of Psychology and Neuroscience, Maastricht University, Universiteitssingel 40 6229 ER Maastricht, The Netherlands; E-Mail: madelon.peters@maastrichtuniversity.nl

* **Correspondence:** Anna Huysse-Gaytandjieva; E-Mail: info@hashimoto.help

Academic Editor: Chris Irons

Special Issue: Compassion Focused Therapy (CFT) - New Insights and Outcomes

OBM Integrative and Complementary Medicine
2022, volume 7, issue 3
doi: 10.21926/obm.icm.2203027

Received: January 09, 2022
Accepted: June 20, 2022
Published: July 12, 2022

Abstract

Hashimoto thyroiditis (HT) is an autoimmune disease affecting mainly middle-aged women. Hormonal replacement is the most common therapy; however, it tackles only the functionality of the thyroid and not the autoimmunity components. Thus, patients experience persistent somatic and psychological symptoms, thereby affecting their quality of life. The cause of HT remains uncertain. Primary evidence suggests that adverse experiences in childhood are associated with autoimmune disease manifestation in adulthood; therefore, the effect of early adverse events on disease course needs to be explored. This paper explored patients' early life events and everyday experiences through the lens of compassion, as defined in compassion-focused therapy (CFT). In this study, nine participants were interviewed, and the transcribed interviews were analyzed using Thematic Analysis. Qualitative analysis indicated that patients exhibited increased psychological distress and a lack of understanding from others. Common patterns of experiences and behaviors were identified, such as the lack of compassion and affiliation between significant others and themselves. Therefore, including psychological care in the therapeutic process of HT would improve patients' well-being and quality of life. In particular, cultivating compassion could be a promising strategy for disease prevention and the healthy functioning of patients.

Keywords

Compassion-focused therapy; CFT; Hashimoto thyroiditis; autoimmune diseases

1. Introduction

Hashimoto thyroiditis (HT) is an autoimmune disease wherein the immune system turns against the thyroid gland. Thyroid cells are destroyed by antibodies, leading to cell death and reduced production of thyroid hormones. HT is the most frequent cause of hypothyroidism in developed countries, with an annual frequency of 0.3–1.5 per 1000 individuals; women are 10 times more vulnerable than men [1-3]. The cause of HT remains uncertain, but both genetic (70%–80%) and environmental (20%–30%) factors, such as smoking, alcohol, and stress, add to HT pathogenesis [4, 5]. Because the initial symptoms are broad and nonspecific, the disease is often diagnosed at a later stage.

Thyroid hormone replacement therapy, which is the standard treatment for HT, combats the insufficient thyroid production. However, this therapy does not address the immune system dysregulation or increased antibody levels. Thus, many patients with HT who are undergoing thyroid hormone replacement therapy still experience persistent symptoms that affect their quality of life. These complaints include physical symptoms, such as constipation, muscle pain, irregular menstrual period, and thyroid gland enlargement; impairments in cognitive functioning; and psychological distress [6, 7]. The psychological symptoms increase with the higher levels of circulating antibodies against thyroid cells [8-10]. In some patients with HT, the psychological symptoms lead to a diagnosis of a mental health disorder [11]. Additionally, because the disease may cause changes in body appearance and anatomy, such as skin dryness, hair loss, weight gain, and hoarseness [12], feelings of shame may occur in patients with HT.

Apart from inducing autoimmune diseases, such as HT, psychological distress affects the course of such diseases. Adverse events and trauma in childhood, which may be caused by inadequate attachment, are associated with an increased prevalence of inflammatory and autoimmune diseases in adulthood [13] as well as higher chances of hospitalization for these diseases [14]. Individuals are born with a natural motivation to seek proximity, protection, and safety from attachment figures (e.g., caregivers) [15]. This behavior results in reduced arousal in light of fear or threat conditions [16]. The extent to which attachment figures are responsive to this proximity-seeking behavior determines the regulation of emotion in infants and shapes their sense of attachment security [17, 18]. The unavailability and unresponsiveness of attachment figures or such figures being a source of threat are associated with an insecure attachment style, thereby eliciting a threat response that invokes anxiety, fear, and distress in prospective experiences [19]. Insecure attachment causes prolonged activation of the hypothalamic–pituitary–adrenal (HPA) axis, thereby resulting in the dysregulation of stress responsivity and uncontrolled inflammation. Insecurelyattached infants may experience more inflammation-related illnesses in adulthood [20]. Furthermore, the incapacity to lower arousal and decrease threat responses harms immune functioning, thereby inducing autoimmunity [21]. Moreover, psychological factors affect the course of autoimmune diseases [22]. For example, negative emotions increase inflammatory responses and aggravate the condition [23]. Shame and threat to the social self are associated with increased cortisol and proinflammatory cytokine activity [24]. This cascade of events affects the course of autoimmune diseases, including HT.

This paper focused on the framework of compassion as established in compassion-focused therapy (CFT). Compassion is defined as "a deep awareness of the suffering of another coupled with the wish to relieve it" [25]. CFT consists of three compassion flows: being compassionate toward others, being receptive to compassion coming from others, and being self-compassionate. Individuals with physical and mental health difficulties may experience elevated threat processing associated with the physiological effects of threat. For example, in addition to the internal threats (e.g., self-criticism), adjusting to and living with a disease generate both acute (e.g., facing a disease diagnosis) and ongoing illness stressors (e.g., threats to social relationships) [26]. These stressors are overwhelming, and trigger sustained activation of the threat system. Compassion helps individuals become mindful of being caught in the threat system and switch attention to a caring and compassionate motivational system; this rebalances the threat system by stimulating physiological systems, such as vagus nerve oxytocin and the frontal cortex, associated with caring [27]. Thus, compassion increases individuals' ability to reduce heightened arousal and threat responses [28]. Compassion helps patients with chronic conditions accept their condition and the associated limitations instead of feeling guilty or blaming themselves [29]. Taken together, compassion assists patients with chronic and autoimmune diseases to better cope with their diseases.

Compassion stems from the affiliating and caring behavior individuals receive during infancy; therefore, it is associated with attachment experiences. Attachment systems determine the development of an affect regulation system that is responsible for allowing capabilities, such as relating to the self in a compassionate manner, experiencing social safeness, and responding with acceptance to being cared for. By extension, infants who experienced limited compassion from their attachment figures might be resistant to accepting compassion from others or themselves as adults. Threat experiences and adverse events in the early years cause individuals to develop blockages and fears of compassion and affect their ability to engage in soothing behaviors [30, 31]. Because autoimmunity has been associated with early adversity, it is interesting to explore the effect of adverse events on HT development and how they may have defined patients' compassionate abilities. Additionally, as compassionate skills and abilities reduce arousal and facilitate soothing, the lack of these would also affect how patients experience their disease and its chronic symptoms.

Here, we examined the general experience of living with HT and how HT influenced patients' relationships with themselves and with others throughout their lives from a compassion framework perspective.

2. Materials and Methods

2.1 Recruitment and Setting

2.1.1 Recruitment

Participants were selected from a large sample of patients participating in a CFT-based intervention that was developed by Hashimoto. Help organization and was delivered online over 6 weeks. Patients were recruited through an internal forum of the Thyroid UK Association and social media channels. Inclusion criteria were: patients with a diagnosis of HT, 18 years or older, good command of English, access to the internet, and good computer literacy. We did not include any exclusion criteria. Seventy-eight patients participated in the online intervention; of whom, nine patients who participated in wider interventions were randomly selected for in-depth interviews.

2.1.2 Participants

All nine participants were females, aged 28–65 years and with a mean age of 48.2 years. Six of them were married, and five were mothers. To initiate the intervention, 78 participants were recruited after filling out the preintervention questionnaires. Upon completing all intervention modules, 22 of these participants filled out the postintervention questionnaires. Nine participants from the initial sample were randomly selected for the interviews. Participants were aware of the purpose of the study. The interviewer was also the instructor of the intervention (2nd author), and the participants were familiar with her through the audio or video recordings that were part of the intervention files.

2.2 Data Collection and Analysis

2.2.1 Materials

After completing the intervention, all participants were interviewed individually by the 2nd author online (video call). A structured format with nine standard open-ended questions was adopted for the interview; additional questions emerged from the participants' answers. The questions focused on patients' experiences of living with HT, compassion, and relationships with others, and their feedback on the intervention. Questions related to feedback and intervention effects were not taken into account in this paper.

2.2.2 Analysis

Data were analyzed using Thematic Analysis, using the step-by-step guide from Braun and Clarke [32]. The person performing the analysis (1st author) was not involved in the interview design and execution and was blind to the intervention during the analysis time. The interviews were transcribed verbatim and read multiple times before coding. After code generation, themes were developed and reviewed.

3. Results

3.1 Qualitative Analysis

Results indicated that participants exhibited both psychological and physical symptoms. Frequently mentioned symptoms included fatigue, anxiety, depression, muscle pain, headache, and sleep problems. In addition, the symptoms affected participants' level of overall functioning, including work ability and intellectual capacity.

Three key themes were identified during the analysis: living under uncertainty, relationship with oneself, and relationship with others.

3.2 Themes and Subthemes

3.2.1 Living Under Uncertainty

<u>Diagnosis Uncertainty.</u> Participants reported that the HT diagnosis was challenging and occurred late. Often, participants initially received another diagnosis, usually for a mental health disorder; some were prescribed antidepressants:

"I was extremely anxious and depressed, and all these things obviously had something to do with the disease, but my doctor didn't understand it, and so I was on antidepressants for a long time." (P1, 52 years)

Participants reported that healthcare professionals view HT as an organ-specific disease and ignore the autoimmunity component. Most of the participants engaged in self-research and self-diagnosis to understand their symptoms:

"It certainly doesn't make sense to any healthcare professional, and I think even to these days, they would say to me 'that's impossible, or I've never heard of it, or that can't be the case.' People don't quite understand or believe that how we feel is actually real to us." (P6, 31 years)

<u>Disease Uncertainty.</u> Eight of nine participants were unsure when the first symptoms appeared or when the disease manifested itself. This inability confused participants' sense of self to the extent that they could not separate the behaviors related to their personality and the ones related to their symptoms:

"I don't know how long I've had Hashimoto's for or for how long my thyroid was impaired. […] I always wondered was I like that because it was just me to be like that or was I like that because actually, it was Hashimoto's making me feel like that? And I still don't know the answer to that." (P3, 32 years)

Participants explained that living with HT resulted in fear of what was coming next related to their health status. This increased health-related anxiety further inhibits stress regulatory systems and aggravates the condition and the immune system dysfunctionality:

"Every day you don't know if your voice is going to be there, whether you're going to be hoarse, whether you're going to be stiff, whether they're going to diagnose you with another autoimmune disease… It's totally unknown." (P5, 45 years)

Because of the sense of not being able to control their symptoms, participants felt uncertainty about their bodies and behavior:

"My daughter was playing in the bath in the evening and I woke up on the bathroom floor. I'd fallen asleep. Fortunately, she was absolutely fine but I thought she could have drowned while I was asleep and didn't watch it – It shocked me and it frightened me." (P4, 57 years)

3.2.2 Relationship With Oneself

Lack of Self-compassion. A common observation in all interviews was participants' belief that past attitudes and ways of life could have been responsible for HT development. This may be because of internalized guilt and self-blame, thereby triggering the threat system and affecting patients physiologically and psychologically:

"Now I got 2 autoimmune disorders. Why? I think stress was a big part of it. A member of my family passed away, it was fast cancer […] suddenly my job came from being comfort zone to this huge world of responsibility [...] my diet wasn't great and you know, my exercise routine wasn't great either. I was in junk food lifestyle." (P3, 32 years)

Participants reported experiencing a lack of self-compassion. Being compassionate toward oneself was viewed by the participants as a sign of self-pity or weakness, which in turn generates negative emotions. This is in line with the research findings that revealed that fears, blocks, or resistances to self-compassion are commonly expressed as shame and self-criticism.

"If I start being nice and feeling sorry for myself, I get upset." (P9, 70 years)
"I think it's a sign of weakness. It's losing control." (P5, 45 years)

This belief was related to high self-expectations and high-performance standards that they had set for themselves:

"Why am I constantly trying to challenge myself, put myself into the most extreme positions just to prove that I can? And again, it all goes back to the fear of inadequacy, lack of self-confidence, not being good enough." (P7, 55 years)

Participants felt responsible for changes in their lives, such as going from full-time to part-time employment to the inability to work at all. Such changes generated guilt and shame as well as worrying about others' perceptions:

"Then I get angry with myself and think 'if everybody else can do it, why can't I go to work? If I needed and I had to, then I would be working! Am I using this as an excuse?' [...] 'Am I just being useless? […] This is not a good role model to give my daughter, you know? She sees that I'm just tired all the time." (P1, 52 years)

Effect of the Disease on Identity and Roles. HT was perceived by participants as part of their identity, and it was not something they liked:

"And I don't want my disease to define me and who I am […] it's a part of me, it's not all of me!" (P4, 57 years)

Most participants explained that HT changed them over the years and affected crucial areas of their lives:

"I'm an intellectual person, and it was very scary when I lost that, and it still is a little bit scary because I'm losing it. Not being able to put words together, in a sense to not be as articulate as I once was." (P7, 55 years)

The way they regulate their emotions and how this has changed over the years also worried participants:

"But the last 5 years I haven't worked and I still react badly to a situation […] And now it's 4 and a half years since I stopped work and I still think I have to be at home in a stressful way." (P2, 60 years)

3.2.3 Relationship With Others

Relationships During Childhood. All participants referred to adverse events in earlier years or right before disease onset that could have played a role in HT development. The most frequently reported events were divorce of parents, abuse, mental health disorder or addiction in the family, abandonment, and limited emotional support. Most participants did not realize that these circumstances might have been traumatic:

"I've always thought I've had a fine childhood. But when I actually tell somebody they go 'that's so traumatic'— I couldn't think about my early childhood for a long time." (P1, 52 years)

Some participants insisted that the adverse events could not be related to their HT development or behavior. Interestingly, some participants even blamed themselves for these events:

"I don't see a problem that, in my earlier days, my brother was always my mother's favorite. You know, he couldn't have done anything wrong. I don't see that as being a lifelong problem that I have. I don't. […] I always got the blame for everything, but that's my fault for not standing up for myself. I can understand now that. But no, I had a nice, I had a nice childhood." (P9, 70 years)

Blocking Compassion Reception. Being compassionate toward oneself has been seen as a form of self-pity. In a similar vein, receiving compassion from others was seen by participants as a lack of independence and a vulnerability trigger; therefore, blocking compassion reception serves as a protective strategy. Moreover, participants reported that they are not open to receiving compassion from others, as they feel like they are being a burden:

"When they want to give me advice or, you know, just do something nice or just reassure me, I kind of probably find it really awkward. And I don't like being a burden, and I think that wasn't… that to me again it's very much linked to Hashimoto's." (P6, 31 years)

Participants also explained that being vulnerable in front of others contradicts their overall self-perception:

"I've always thought myself as being quite tough I suppose. But I'm not really. Every time anybody's being nice to me and comforting me or whatever, something's going wrong, I'm just bursting to tears, I can't control that." (P9, 70 years)

Another common explanation for limited openness to others was a lack of trust in others, which was related to past experiences:

"I would probably feel the very same as I did back then. And it takes a lot to me to trust people now because I'm not gonna give you all of me for you to then say no I don't want you anymore, go away!" (P3, 32 years)

Limited openness was linked to certain personality patterns. The most common patterns included high self-expectations, perfectionism, guilt, self-consciousness and anticipated shame, conflict, rejection, and vulnerability avoidance:

"I should be strong and you shouldn't need to help me or care for me or hug me and make me feel better because I should be able to deal with things […] I'm a bit of a perfectionist […] I don't want to feel shame and ask for help either." (P3, 32 years)

<u>Not Feeling Understood.</u> All participants explained that they lack a sense of understanding from others. Close relations do not take the disease and its effects seriously. Instead, they label them as overreactive and oversensitive rather than attributing their symptoms to the disease:

"I know in my body that that was causing the problem and everyone else's convinced I'm having a breakdown because my dog died, or my friend died, or my mother died, without actually considering that it might be anything else. And that in itself is upsetting." (P9, 70 years)

Because individuals without HT do not show understanding, not knowing other patients resulted in some participants feeling isolated:

"I don't know anyone personally with Hashimoto's and it's one of those very strange things you can't explain to people because it just sounds like you're being lazy or flaky or mad. It's very difficult for anyone to understand it." (P8, 50 years)

Two participants elaborated on not being understood, explaining that the reason may be their own inability to open up. This could be related to fears of receiving compassion from others, which they struggled with:

"And then I question myself why should I be frustrated if my friends don't understand? Then I realize I don't tell them. I don't share with them. I don't help them understand. I just get very annoyed when they do it." (P3, 32 years)

Participants explained that they noticed changes in socializing after HT development. This seemed to be generated by heightened self-consciousness and HT symptoms, such as fatigue, anxiety, and sleeplessness, that drain their energy and impede them from socializing:

"I struggle to talk to people actually. I find that I've got not really much to say. And I think it's just because I'm so exhausted, I wish I had the energy for communicating to strangers." (P8, 50 years)

4. Discussion

In CFT, compassion is defined as "a sensitivity to suffering in self and others, with a commitment to try to alleviate and prevent it" [33]. If the three themes derived from the data are related to the CFT model, it indicates that uncertainty activates the threat system; therefore, the requirement for the regulatory capacities of the soothing system arises (relationship with oneself and others). Participants of this study experienced somatic symptoms, negative emotions, and an inability to live up to expected standards (e.g., having a job). HT and changes in life after diagnosis create a vicious cycle. Participants believed that their inability to regulate negative emotions or their involvement in stressful situations elicited the autoimmune response. HT symptoms, such as fatigue and weakness, impeded participants from performing everyday activities. HT development also created uncertainty about developing another autoimmune disease. Thus, patients with HT keep circling around the threat system. All participants reported that these challenges were overlooked by significant others, such as the wider social community and especially healthcare professionals who focus solely on organ functionality, leaving them feeling alone and unable to exit the threat system.

Participants generally lacked self-compassion and the ability to stay open to receive compassion from others. They blamed themselves for developing HT and for the effect of symptoms on their functioning. These internal threats activated their threat system. Their difficulty in receiving compassion may be rooted in early adverse events. Almost all participants reported experiencing traumatic events in early childhood, characterized by neglect or maltreatment. Tendencies, such as pleasing others and seeking approval, may be associated with how the attachment and soothing system have developed; this is more relevant to the soothing system as it is related to the threat system. Several studies have suggested that early life stress induces brain alterations and immune dysregulation [34] and enhances the proinflammatory tendency of cells [35]; therefore, whether early adversity also contributes to the etiology of HT should be further examined.

This study provides preliminary evidence that patients with HT often report low compassion, which may be associated with early adverse events and insecure attachment. Therefore, patients with HT may benefit from a CFT-based intervention. CFT can help them broaden their understanding of compassion, work with current blocks, and develop a soothing compassionate system. This, in turn, can activate the soothing system without triggering the threat system. Currently, no permanent cure for HT exists. In this scenario, CFT can help patients with HT to reconcile themselves with their disease by developing compassion and sensitivity to one's suffering. Moreover, CFT-based interventions may alleviate HT symptoms by reducing physiological stress responses. Engaging in compassion-focused meditation reduces the levels of stress-induced proinflammatory cytokines

[36]. A limitation of this study was that the interviews were conducted after a CFT intervention was administered to the participants. Therefore, some components of the intervention (e.g., mindfulness techniques) may have enhanced participants' awareness, and some may have reactivated memories of the attachment system. As a result, participants' responses during the interviews may have been affected. Nevertheless, the increased awareness or negative memories may have facilitated the provision of their insights as well.

5. Conclusions

This study revealed some common patterns in patients with HT, such as lack of compassion, feelings of isolation, and increased anxiety. Patients with HT report lifelong symptoms, including psychological distress, that are often neglected by healthcare professionals. Cultivating compassion could be a promising method to alleviate HT symptoms by reducing anxiety and physiological stress responses. Furthermore, including psychological care in general, and compassion in particular, in the therapeutic process of HT would improve the symptoms of patients who downregulate negative emotions and promote positive emotions.

Acknowledgments

We would like to thank the Thyroid UK Association for announcing the research among their members.

Author Contributions

Conceived and designed the study, build the intervention, interviewed the participants: AHG; performed the qualitative analysis and wrote the manuscript: ZP; Co-designed the study, performed the quantitative data analyses, and collaborated in the writing and editing of the final manuscript: MLP; All authors approved the final version of the manuscript for submission.

Competing Interests

AHG is founder and director of Hashimoto.Help. Hashimot.Help is a non-profit organization offering evidence-based services aimed at 1) the early detection and prevention of Hashimoto Thyroiditis and 2) the improvement of the quality of life of patients with Hashimoto Thyroiditis. MP is part of the advisory board of Hashimoto.Help. ZP has nothing to disclose.

References

1. Mincer DL, Jialal I. Hashimoto thyroiditis. In: StatPearls. Treasure Island: StatPearls Publishing LLC; 2020.
2. Caturegli P, De Remigis A, Rose NR. Hashimoto thyroiditis: Clinical and diagnostic criteria. Autoimmun Rev. 2014; 13: 391-397.
3. Ramos Leví AM, Marazuela M. Pathogenesis of thyroid autoimmune disease: The role of cellular mechanisms. Endocrinol Nutr. 2016; 63: 421-429.
4. Rogers MP, Fozdar M. Psychoneuroimmunology of autoimmune disorders. Adv Neuroimmunol. 1996; 6: 169-177.

5. Wiersinga WM. Clinical relevance of environmental factors in the pathogenesis of autoimmune thyroid disease. Endocrinol Metab. 2016; 31: 213-222.
6. Djurovic M, Pereira AM, Smit JWA, Vasovic O, Damjanovic S, Jemuovic Z, et al. Cognitive functioning and quality of life in patients with Hashimoto thyroiditis on long-term levothyroxine replacement. Endocrine. 2018; 62: 136-143.
7. Samuels MH, Schuff KG, Carlson NE, Carello P, Janowsky JS. Health status, psychological symptoms, mood, and cognition in L-thyroxine-treated hypothyroid subjects. Thyroid. 2007; 17: 249-258.
8. Uysal HB, Ayhan M. Autoimmunity affects health-related quality of life in patients with Hashimoto's thyroiditis. Kaohsiung J Med Sci. 2016; 32: 427-433.
9. Müssig K, Künle A, Säuberlich AL, Weinert C, Ethofer T, Saur R, et al. Thyroid peroxidase antibody positivity is associated with symptomatic distress in patients with Hashimoto's thyroiditis. Brain Behav Immun. 2012; 26: 559-563.
10. Ott J, Promberger R, Kober F, Neuhold N, Tea M, Huber JC, et al. Hashimoto's thyroiditis affects symptom load and quality of life unrelated to hypothyroidism: A prospective case-control study in women undergoing thyroidectomy for benign goiter. Thyroid. 2011; 21: 161-167.
11. Carta MG, Hardoy MC, Carpiniello B, Murru A, Marci AR, Carbone F, et al. A case control study on psychiatric disorders in Hashimoto disease and euthyroid goitre: Not only depressive but also anxiety disorders are associated with thyroid autoimmunity. Clin Pract Epidemiol Ment Health. 2005; 1: 23.
12. Barić A, Brčić L, Gračan S, Škrabić V, Brekalo M, Šimunac M, et al. Thyroglobulin antibodies are associated with symptom burden in patients with hashimoto's thyroiditis: A cross-sectional study. Immunol Invest. 2019; 48: 198-209.
13. Schubert C. Psychoneuroimmunology of the life span: Impact of childhood stress on immune dysregulation and inflammatory disease in later life. Psychother Psychosom Med Psychol. 2014; 64: 171-180.
14. Dube SR, Fairweather D, Pearson WS, Felitti VJ, Anda RF, Croft JB. Cumulative childhood stress and autoimmune diseases in adults. Psychosom Med. 2009; 71: 243-250.
15. Bowlby J. Attachment and loss: Volume II: Separation, anxiety and anger. In: Attachment and loss: Volume II: Separation, anxiety and anger. London: Penguin; 1973.
16. Gilbert P. Compassion: From its evolution to a psychotherapy. Front Psychol. 2020; 11: 586161.
17. Ainsworth MD. Attachments across the life span. Bull N Y Acad Med. 1985; 61: 792-812.
18. Bowlby J. The bowlby-ainsworth attachment theory. Behav Brain Sci. 1979; 2: 637-638.
19. Mikulincer M, Shaver PR. Boosting attachment security to promote mental health, prosocial values, and inter-group tolerance. Psychol Inq. 2007; 18: 139-156.
20. Puig J, Englund MM, Simpson JA, Collins WA. Predicting adult physical illness from infant attachment: A prospective longitudinal study. Health Psychol. 2013; 32: 409.
21. Schore AN. Affect regulation and the origin of the self: The neurobiology of emotional development. Hillsdale: L. Erlbaum Associates; 1994.
22. Ziemssen T. Psychoneuroimmunology - psyche and autoimmunity. Curr Pharm Des. 2012; 18: 4485-4488.
23. Moons WG, Eisenberger NI, Taylor SE. Anger and fear responses to stress have different biological profiles. Brain Behav Immun. 2010; 24: 215-219.

24. Dickerson SS, Gruenewald TL, Kemeny ME. When the social self is threatened: Shame, physiology, and health. J Pers. 2004; 72: 1191-1216.
25. Gilbert P. Introducing compassion-focused therapy. Adv Psychiatr Treat. 2009; 15: 199-208.
26. Dekker J, de Groot V. Psychological adjustment to chronic disease and rehabilitation–an exploration. Disabil Rehabil. 2018; 40: 116-120.
27. Porges SW. Vagal pathways: Portals to compassion. In: The Oxford handbook of compassion science. Oxford: Oxford University Press; 2017. pp.189-202.
28. Gilbert P. The evolution of shame as a marker for relationship security: A biopsychosocial approach. In: The self-conscious emotions: Theory and research. New York: Guilford Press; 2007. pp.283-309.
29. Austin J, Drossaert CHC, Schroevers MJ, Sanderman R, Kirby JN, Bohlmeijer ET. Compassion-based interventions for people with long-term physical conditions: A mixed methods systematic review. Psychol Health. 2021; 36: 16-42.
30. Gilbert P, McEwan K, Matos M, Rivis A. Fears of compassion: Development of three self-report measures. Psychol Psychothe Theory Res Pract. 2011; 84: 239-255.
31. Matos M, Duarte J, Pinto Gouveia J. The origins of fears of compassion: Shame and lack of safeness memories, fears of compassion and psychopathology. J Psychol. 2017; 151: 804-819.
32. Braun V, Clarke V. Using thematic analysis in psychology. Qual Res Psychol. 2006; 3: 77-101.
33. Gilbert P. The origins and nature of compassion focused therapy. Br J Clin Psychol. 2014; 53: 6-41.
34. Agorastos A, Pervanidou P, Chrousos GP, Baker DG. Developmental trajectories of early life stress and trauma: A narrative review on neurobiological aspects beyond stress system dysregulation. Front Psychiatry. 2019; 10: 118.
35. Miller GE, Chen E, Parker KJ. Psychological stress in childhood and susceptibility to the chronic diseases of aging: Moving toward a model of behavioral and biological mechanisms. Psychol Bull. 2011; 137: 959-997.
36. Pace TW, Negi LT, Adame DD, Cole SP, Sivilli TI, Brown TD, et al. Effect of compassion meditation on neuroendocrine, innate immune and behavioral responses to psychosocial stress. Psychoneuroendocrinology. 2009; 34: 87-98.